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=> e fahey robert c/au
E1          6   FAHEY RICHARD P/AU
E2          1   FAHEY RICHARD PATRICK/AU
E3        123 --> FAHEY ROBERT C/AU
E4          5   FAHEY ROBERT E/AU
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E6          1   FAHEY ROBERT W C/AU
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E9          4   FAHEY S A/AU
E10         1   FAHEY S F/AU
E11         2   FAHEY S H/AU
E12         1   FAHEY S J/AU

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L1         21 "FAHEY ROBERT C"/AU AND MYCO?

=> dup rem l1
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L2         14 DUP REM L1 (7 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 14 ANSWERS - CONTINUE? Y/(N):y

L2  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2002 ACS
AN  2001:923972  CAPLUS
DN  136:66199
TI  ***Mycobacterial***  acetylglucosaminylinositol deacetylase is a
    ***mycothiol***  biosynthetic enzyme with analytical and antimicrobial
    inhibitor design uses
IN  Newton, Gerald L.; Av-Gay, Yossef;  ***Fahey, Robert C.***
PA  The Regents of the University of California, San Diego, USA; University of
    British Columbia
SO  PCT Int. Appl., 92 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE        APPLICATION NO.  DATE
    --------------  ----  --------    ---------------  --------
PI  WO 2001096529   A2    20011220    WO 2001-US19091  20010614
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
           CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
           GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
           LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
           RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
           UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
           DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
           BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-211612P  P   20000614
AB  The present invention provides a family of bacterial
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acetylglucosaminylinositol deacetylases (MshB) with deacetylase activity against acylglucosaminylinositol and which play a key role in ***mycothiol*** biosynthesis. The invention deacetylases are characterized by a conserved 100 amino acid N-terminal region and 3 highly conserved histidine-contg. regions and by having deacetylase activity as well as amide hydrolase activity. The invention further provides methods for using the invention deacetylases in drug screening assays to det. compds. that inhibit activity. The invention provides for treatment of actinomycete infections in mammals using antibiotics that inhibit prodn. or activity of MshB and thereby reduce the prodn. of ***mycothiol*** and the virulence of the infecting bacteria.

L2 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:435230 CAPLUS
DN 135:57858
TI Bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification
IN Newton, Gerald L.; Av-gay, Yossef; ***Fahey, Robert C.***
PA The Regents of the University of California, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001042422	A2	20010614	WO 2000-US33232	20001207
WO 2001042422	A3	20020110		
AU 2001020702	A5	20010618	AU 2001-20702	20001207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-169503P A2 19991207
WO 2000-US33232 W 20001207
AB The present invention provides a family of bacterial acyl glucosaminyl inositol amidases with amidase activity against S-conjugate amides, particularly ***mycothiol*** -derived S-conjugate amides. The invention amidases are characterized by a highly conserved 20 amino acid N-terminal region and four highly conserved histidine-contg. regions and by having amidase activity, particularly amide hydrolase activity. Purifn., characterization and sequences of ***mycothiol*** S-conjugate amidases of ***Mycobacterium*** smegmatis mc2 155 and M. tuberculosis H37Rv (Rv1082) are disclosed. The invention further provides methods for using the invention amidases in drug screening assays to det. compds. with antibiotic activity or compds. that inhibit activity or prodn. of endogenous acyl glucosaminylinositol amidase in bacteria. The invention further provides methods for detoxifying a toxic substance by contacting the toxic substance with an invention amidase, for example, by expression

of the amidase under environmental conditions in a bacterium.

L2 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:201920 BIOSIS
DN PREV200200201920
TI Novel thiols of prokaryotes.
AU ***Fahey, Robert C. (1)***
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093: rcfahey@ucsd.edu USA
SO Ornston, L. Nicholas [Editor]; Balows, Albert [Editor]; Gottesman, Susan [Editor]. Annual Review of Microbiology, (2001) Vol. 55, pp. 333-356. Annual Review of Microbiology. print.
Publisher: Annual Reviews 4139 El Camino Way, Palo Alto, CA, 94303-0139, USA.
ISSN: 0066-4227.
DT Book
LA English

L2 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:288460 CAPLUS
DN 135:31474
TI Novel bromotyrosine alkaloids: Inhibitors of ***mycothiol*** S-conjugate amidase
AU Nicholas, Gillian M.; Newton, Gerald L.; ***Fahey, Robert C.*** ; Bewley, Carole A.
CS Laboratory of Bioorganic Chemistry, NIDDK National Institutes of Health, Bethesda, MD, 20892-0820, USA
SO Organic Letters (2001), 3(10), 1543-1545
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
AB The novel alkaloids (I) and (II) were isolated from an Australian non-verongid sponge, Oceanapia sp. Compd. I contains an unprecedented imidazolyl-quinolinone substructure attached to a bromotyrosine-derived spiro-isoxazoline. Three other known alkaloids were isolated in addn. to I and II and together represent the first examples of inhibitors of a new ***mycobacterial*** enzyme ***mycothiol*** S-conjugate amidase (MCA).
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:776059 CAPLUS
DN 136:34381
TI Novel thiols of prokaryotes
AU ***Fahey, Robert C.***
CS Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093, USA
SO Annual Review of Microbiology (2001), 55, 333-356
CODEN: ARMIAZ; ISSN: 0066-4227
PB Annual Reviews Inc.
DT Journal; General Review
LA English
AB A review. Glutathione metab. is assocd. with oxygenic cyanobacteria and

the oxygen-utilizing purple bacteria, but is absent in many other prokaryotes. This review focuses on novel thiols found in those bacteria lacking glutathione. Included are glutathione amide and its perthiol, produced by phototrophic purple sulfur bacteria and apparently involved in their sulfide metab. Among archaebacteria, coenzyme M (2-mercaptoethanesulfonic acid) and coenzyme B (7-mercaptoheptanoylthreonine phosphate) play central roles in the anaerobic prodn. of CH4 and assocd. energy conversion by methanogens, whereas the major thiol in the aerobic phototrophic halobacteria is .gamma.-glutamylcysteine. The highly aerobic actinomycetes produce ***mycothiol*** , a conjugate of N-acetylcysteine with a pseudodisaccharide of glucosamine and myo-inositol, AcCys-GlcN.alpha.(1 .fwdarw. 1)Ins, which appears to play an antioxidant role similar to glutathione. Ergothioneine, also produced by actinomycetes, remains a mystery despite many years of study. Available data on the biosynthesis and metab. of these and other novel thiols is summarized and key areas for addnl. study are identified.

RE.CNT 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AN 2000:439612 BIOSIS

DN PREV200000439612

TI A novel ***mycothiol*** -dependent detoxification pathway in ***mycobacteria*** involving ***mycothiol*** S-conjugate amidase.

AU Newton, Gerald L.; Av-Gay, Yossef; ***Fahey, Robert C. (1)***

CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093 USA

SO Biochemistry, (September 5, 2000) Vol. 39, No. 35, pp. 10739-10746. print. ISSN: 0006-2960.

DT Article

LA English

SL English

AB ***Mycothiol*** , 1-D-myo-inosityl-2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (MSH), is composed of N-acetylcysteine (AcCys) amide linked to 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (GlcN-Ins) and is the major thiol produced by most actinomycetes. When ***Mycobacterium*** smegmatis was treated with the alkylating agent monobromobimane (mBBr), the cellular ***mycothiol*** was converted to its bimane derivative (MSmB). The latter was rapidly cleaved to produce GlcN-Ins and the bimane derivative of N-acetylcysteine (AcCySmB), a mercapturic acid that was rapidly exported from the cells into the medium. The other product of cleavage, GlcN-Ins, was retained in the cell and utilized in the resynthesis of ***mycothiol*** . The ***mycothiol*** S-conjugate amidase (amidase) responsible for cleaving MSmB was purified to homogeneity from M. smegmatis. A value of Km = 95 +- 8 muM and a value of kcat = 8 s-1 was determined for the amidase with MSmB as substrate. Activity with 100 muM ***mycothiol*** or with the monobromobimane derivative of 1-D-myo-inosityl-2-(L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (CySmB-GlcN-Ins) or of 2-(N-acetyl-L-cysteinyl)amido-2-deoxy-(alpha,beta)-D-glucopyranoside (AcCySmB-GlcN) was at least 103 lower than with 100 muM MSmB, demonstrating that the amidase is highly specific for S-conjugates of ***mycothiol*** . Conjugates of ***mycothiol*** with the antibiotic cerulenin, N-ethylmaleimide, 3-(N-maleimidopropionyl)-

biocytin, and 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin also exhibited significant activity. The sequence of the amino-terminal 20 residues was determined, and an open reading frame (Rv1082) coding for 288 residues having an identical predicted amino-terminal amino acid sequence was identified in the ***Mycobacterium*** tuberculosis genome. The Rv1082 gene (mca) from M. tuberculosis was cloned and expressed in Escherichia coli, and the expressed protein was shown to have substrate specificity similar to the amidase from M. smegmatis. These results indicate that ***mycothiol*** and ***mycothiol*** S-conjugate amidase play an important role in the detoxification of alkylating agents and antibiotics.

L2 ANSWER 7 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:313790 BIOSIS
DN PREV200100313790
TI N-acetyl-1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside deacetylase (MshB) is a key enzyme in ***mycothiol*** biosynthesis.
AU Newton, Gerald L.; Av-Gay, Yossef; ***Fahey, Robert C. (1)***
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506: rcfahey@ucsd.edu USA
SO Journal of Bacteriology, (December, 2000) Vol. 182, No. 24, pp. 6958-6963. print.
ISSN: 0021-9193.
DT Article
LA English
SL English
AB ***Mycothiol*** is a novel thiol produced only by actinomycetes and is the major low-molecular-weight thiol in ***mycobacteria*** . ***Mycothiol*** was previously shown to be synthesized from 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside by ligation with cysteine followed by acetylation. A novel ***mycothiol*** -dependent detoxification enzyme, ***mycothiol*** conjugate amidase, was recently identified in ***Mycobacterium*** smegmatis and shown to have a homolog, Rv1082, in ***Mycobacterium*** tuberculosis. In the present study we found that a protein encoded by the M. tuberculosis open reading frame Rv1170, a homolog of Rv1082, possesses weak ***mycothiol*** conjugate amidase activity but shows substantial deacetylation activity with 1-D-myo-inosityl-2-acetamido-2-deoxy-alpha-D-glucopyranoside (GlcNAc-Ins), a hypothetical ***mycothiol*** biosynthetic precursor. The availability of this protein enabled us to develop an assay for GlcNAc-Ins, which was used to demonstrate that GlcNAc-Ins is present in M. smegmatis at a level about twice that of ***mycothiol*** . It was shown that GlcNAc-Ins is absent in ***mycothiol*** -deficient mutant strain 49 of M. smegmatis and that this strain can concentrate GlcNAc-Ins from the medium and convert it to ***mycothiol*** . This demonstrates that GlcNAc-Ins is a key intermediate in the pathway of ***mycothiol*** biosynthesis. Assignment of Rv1170 as the gene coding the deacetylase in the M. tuberculosis genome represents the first identification of a gene of the ***mycothiol*** biosynthesis pathway. The presence of a large cellular pool of substrate for this enzyme suggests that it may be important in regulating ***mycothiol*** biosynthesis.

L2 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS

DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of ***mycothiol*** and precursors thereof
IN ***Fahey, Robert C.*** ; Newton, Gerald L.; Unson, Maria Margarita D.; Davis, Charles E.; Angerberg, Sara J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921580	A1	19990506	WO 1998-US22577	19981023
AU 9911988	A1	19990517	AU 1999-11988	19981023

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting ***mycothiol*** or precursor thereof. An antibody is provided which binds to ***mycothiol*** or a ***mycothiol*** precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of ***mycothiol*** or a precursor thereof. A method is provided for detecting ***mycothiol*** or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of ***mycothiol*** or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1999:310093 BIOSIS
DN PREV199900310093
TI Improved methods for immunoassay of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Arnold, Karen F.; Davis, Charles E.; ***Fahey, Robert C. (1)***
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506 USA
SO Journal of Clinical Microbiology, (July, 1999) Vol. 37, No. 7, pp. 2153-2157.
ISSN: 0095-1137.
DT Article
LA English
SL English
AB Improved enzyme-linked immunosorbent assay (ELISA) methods have been developed for the determination of femtomole amounts of ***mycothiol***

(MSH), the main low-molecular-weight thiol in ***mycobacteria*** . The immunoassays utilize an affinity-purified rabbit polyclonal antibody that is highly specific for the pseudodisaccharide moiety of MSH. MSH was first biotinylated by the thiol-specific reagent 3-(N-maleimidopropionyl)biocytin. The MSH-biotin adduct was then captured with immobilized avidin and detected with anti-MSH antibody (biotin-capture ELISA) or was captured with immobilized anti-MSH antibody and detected with alkaline phosphatase-labelled avidin (MSH-capture ELISA). The MSH-capture ELISA was the most sensitive method, measuring as little as 0.3 fmol of MSH. Methods for biotinylating MSH directly from ***Mycobacterium*** spp. are described. The MSH-capture ELISA was tested for the detection of M. avium seeded in human urine or cerebrospinal fluid samples and for screening mutant M. smegmatis strains to detect MSH production.

L2 ANSWER 10 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 1999:148924 BIOSIS
DN PREV199900148924
TI Characterization of ***Mycobacterium*** smegmatis mutants defective in 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside and ***mycothiol*** biosynthesis.
AU Newton, Gerald L.; Unson, Mia D.; Anderberg, Sara J.; Aguilera, Joseph A.; Oh, Nancy N.; Delcardayre, Stephen B.; Av-Gay, Yossef; ***Fahey, Robert*** *** C. (1)***
CS (1) Dep. Chem. Biochemistry, Univ. California, San Diego, La Jolla, CA 92093 USA
SO Biochemical and Biophysical Research Communications, (Feb. 16, 1999) Vol. 255, No. 2, pp. 239-244.
ISSN: 0006-291X.
DT Article
LA English
AB ***Mycothiol*** (MSH) is the major low molecular weight thiol in ***mycobacteria*** . Two chemical mutants with low MSH and one with no MSH (strain 49) were produced in ***Mycobacterium*** smegmatis mc2155 to assess the role of MSH in ***mycobacteria*** . Strain 49 was shown to not produce 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (GlcN-Ins), an intermediate in MSH biosynthesis. Relative to the parent strain, mutant 49 formed colonies more slowly on solid media and was more sensitive to H2O2, and rifampin, but less sensitive to isoniazid. Complementation of mutant 49 with DNA from M. tuberculosis H37Rv partially restored production of GlcN-Ins and MSH, and resistance to H2O2, but largely restored colony growth rate and sensitivity to rifampin and isoniazid. The results indicate that MSH and GlcN-Ins are not essential for in vitro survival of ***mycobacteria*** but may play significant roles in determining the sensitivity of ***mycobacteria*** to environmental toxins.

L2 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1999:5037 BIOSIS
DN PREV199900005037
TI ***Mycothiol*** biosynthesis and metabolism: Cellular levels of potential intermediates in the biosynthesis and degradation of ***mycothiol*** in ***Mycobacterium*** smegmatis.

AU Anderberg, Sara J.; Newton, Gerald L.; ***Fahey, Robert C. (1)***
CS (1) Dep. Chem. Biochem., Univ. Calif. at San Diego, La Jolla, CA 92093-0506 USA
SO Journal of Biological Chemistry, (Nov. 13, 1998) Vol. 273, No. 46, pp. 30391-30397.
ISSN: 0021-9258.
DT Article
LA English
AB ***Mycothiol*** (MSH; 1-D-myo-inosityl-2-(N-acetyl-L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (AcCys-GlcN-Ins)) is a novel thiol produced at millimolar levels by ***mycobacteria*** and other actinomycetes that do not make glutathione. We developed methods to determine the major components of MSH (AcCys, Cys-GlcN, AcCys-GlcN, Cys-GlcN-Ins, GlcN-Ins) in cell extracts. ***Mycobacterium*** smegmatis was shown to produce measurable levels (nmol/g of residual dry weight) of AcCys (apprx30), Cys-GlcN-Ins (apprx8), and GlcN-Ins (apprx100) but not Cys-GlcN (<3) or AcCys-GlcN (<80) during exponential growth in Middlebrook 7H9 medium. The level of GlcN-Ins declined 10-fold in stationary phase and apprx5-fold in 7H9 medium lacking glucose. Incubation in 10 mM AcCys produced 50- and 1000-fold increases in cellular Cys and AcCys levels, respectively, a 10-fold decrease in GlcN-Ins and a transient 3-fold increase in Cys-GlcN-Ins. These results exclude Cys-GlcN and AcCys-GlcN as intermediates in MSH biosynthesis and implicate GlcN-Ins and Cys-GlcN-Ins as key intermediates. Assay of GlcN-Ins/ATP-dependent ligase activity with Cys and AcCys as substrates revealed that Cys was at least an order of magnitude better substrate. Based on the cellular measurements, MSH biosynthesis involves assembly of GlcN-Ins, ligation with Cys to produce Cys-GlcN-Ins, and acetylation of the latter to produce MSH.

L2 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 1998:386859 BIOSIS
DN PREV199800386859
TI An immunoassay for the detection and quantitative determination of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Davis, Charles; ***Fahey, Robert C.*** *** (1)***
CS (1) Dep. Chem. and Biochem., Univ. Calif., San Diego, La Jolla, CA 92093 USA
SO Journal of Immunological Methods, (May 1, 1998) Vol. 214, No. 1-2, pp. 29-39.
ISSN: 0022-1759.
DT Article
LA English
AB ***Mycothiol*** (MSH) is a glycosylated derivative of V-acetylcysteine that may have antioxidant functions in ***mycobacteria*** and other actinomycetes. To develop a highly specific assay for MSH, we capitalized on the selective binding of thiols to a maleimide residue linked to bovine serum albumin and employed affinity-purified polyclonal antibody and an enzyme-linked secondary antibody for detection. The assay was shown to be specific and to detect MSH at levels as low as 0.1 pmol when conducted in the form of a microtiter plate-based ELISA. A similar, nitrocellulose membrane-based immunoassay was shown to be useful for qualitative detection of MSH-producing bacterial colonies.

L2 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
AN 1996:232911 BIOSIS
DN PREV199698797040
TI Distribution of thiols in microorganisms: ***Mycothiol*** is a major thiol in most actinomycetes.
AU Newton, Gerald L.; Arnold, Karen; Price, Mitchel S.; Sherrill, Christopher; Delcardayre, Stephen B.; Aharonowitz, Yair; Cohen, Gerald; Davies, Julian; ***Fahey, Robert C. (1)*** ; Davis, Charles
CS (1) Dep. Chemistry, University California, San Diego, La Jolla, CA 92093-0506 USA
SO Journal of Bacteriology, (1996) Vol. 178, No. 7, pp. 1990-1995. ISSN: 0021-9193.
DT Article
LA English
AB ***Mycothiol*** (2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranosyl-(1 fwdarw 1)-myo-inositol) (MSH) has recently been identified as a major thiol in a number of actinomycetes (S. Sakuda, Z.-Y. Zhou, and Y. Yamada, Biosci. Biotech. Biochem. 58:1347-1348, 1994; H. S. C. Spies and D. J. Steenkamp, Eur. J. Biochem. 224:203213, 1994; and G. L. Newton, C. A. Bewley, T. J. Dwyer, R. Horn, Y. Aharonowitz, G. Cohen, J. Davies, D. J. Faulkner, and R. C. Fahey, Eur. J. Biochem. 230:821-825, 1995). Since this novel thiol is more resistant than glutathione to heavy-metal ion-catalyzed oxidation, it seems likely to be the antioxidant thiol used by aerobic gram-positive bacteria that do not produce glutathione (GSH). In the present study we sought to define the spectrum of organisms that produce MSH. GSH was absent in all actinomycetes and some of the other gram-positive bacteria studied. Surprisingly, the streptococci and enterococci contained GSH, and some strains appeared to synthesize it rather than import it from the growth medium. MSH was found at significant levels in most actinomycetes examined. Among the actinobacteria four Micrococcus species produced MSH, but MSH was not found in representatives of the Arthrobacter, Agromyces, or Actinomyces genera. Of the nocardioforms examined, Nocardia, Rhodococcus, and ***Mycobacteria*** spp. all produced MSH. In addition to the established production of MSH by streptomycetes, we found that Micromonospora, Actinomadura, and Nocardiopsis spp. also synthesized MSH. ***Mycothiol*** production was not detected in Propionibacterium acnes or in representative species of the Listeria, Staphylococcus, Streptococcus, Enterococcus, Bacillus, and Clostridium genera. Examination of representatives of the cyanobacteria, purple bacteria, and spirochetes also gave negative results, as did tests of rat liver, bonito, Candida albicans, Neurospora crassa, and spinach leaves. The results, which indicate that MSH production is restricted to the actinomycetes, could have significant implications for the detection and treatment of infections with actinomycetes, especially those caused by ***mycobacteria*** .

L2 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 1995:630956 CAPLUS
DN 124:140470
TI The structure of U17 isolated from Streptomyces clavuligerus and its properties as an antioxidant thiol
AU Newton, Gerald L.; Bewley, Carole A.; Dwyer, Tammy J.; Horn, Ronda; Aharonowitz, Yair; Cohen, Gerald; Davies, Julian; Faulkner, D. John;

Fahey, Robert C.

CS Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506, USA

SO Eur. J. Biochem. (1995), 230(2), 821-5
CODEN: EJBCAI; ISSN: 0014-2956

DT Journal

LA English

AB The predominant low-mol.-mass thiol produced by streptomycetes is a cysteine deriv. previously designated as U17. In this study the elucidation of the structure of the monobromobimane deriv. of U17 (I) is reported, which establishes the structure of U17 as 2-(N-acetylcysteinyl)amido-2-deoxy-.alpha.-D-glucopyranosyl-myo-inositol. The presence of the N-acetylcysteine moiety was indicated by formation of N-acetylcysteine-monobromobimane during acid hydrolysis of I. Complete hydrolysis of I released 1 mol glucosamine/mol cysteine as detd. by carbohydrate and amino acid anal. High-resoln. mass spectral anal. gave a precise mass consistent with the mol. formula C27H40N4O14S. Anal. of 13C-NMR, 1-dimensional 1H-NMR and 2-dimensional NMR expts. identified the remaining C6H12O6 moiety as myo-inositol, confirmed the presence of N-acetyl-cysteine and glucosamine, and established the connectivity of the components. Two chem. properties of this novel thiol, which is equated to ***mycothiol*** from ***Mycobacterium*** bovis, make it suitable as an intracellular storage form of cysteine and as an antioxidant thiol. First, it undergoes heavy-metal-ion catalyzed autoxidn. at a rate dramatically lower than that for cysteine and markedly lower than that for glutathione or N-acetylcysteine. Secondly, the .alpha.-(1.fwdarw.1) glycosidic link between glucosamine and myo-inositol is resistant to acid hydrolysis, hydrolyzing at a rate comparable to that of the 2 amide bonds in the mol.

=> e newton gerald l/au
E1 4 NEWTON GERALD H/AU
E2 1 NEWTON GERALD HARVEY/AU
E3 71 --> NEWTON GERALD L/AU
E4 4 NEWTON GERALD S/AU
E5 1 NEWTON GERRY H/AU
E6 9 NEWTON GILES H/AU
E7 1 NEWTON GINA/AU
E8 2 NEWTON GINA M/AU
E9 3 NEWTON GLEN/AU
E10 1 NEWTON GLEN E/AU
E11 1 NEWTON GONCALVES LADEIRA/AU
E12 1 NEWTON GOODWIN/AU

=> s e3 and myco?
L3 19 "NEWTON GERALD L"/AU AND MYCO?

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 12 DUP REM L3 (7 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:923972 CAPLUS
DN 136:66199
TI ***Mycobacterial*** acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with analytical and antimicrobial inhibitor design uses
IN ***Newton, Gerald L.*** ; Av-Gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, San Diego, USA; University of British Columbia
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096529	A2	20011220	WO 2001-US19091	20010614

PI WO 2001096529 A2 20011220 WO 2001-US19091 20010614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-211612P P 20000614
AB The present invention provides a family of bacterial acetylglucosaminylinositol deacetylases (MshB) with deacetylase activity against acylglucosaminylinositol and which play a key role in ***mycothiol*** biosynthesis. The invention deacetylases are characterized by a conserved 100 amino acid N-terminal region and 3 highly conserved histidine-contg. regions and by having deacetylase activity as well as amide hydrolase activity. The invention further provides methods for using the invention deacetylases in drug screening assays to det. compds. that inhibit activity. The invention provides for treatment of actinomycete infections in mammals using antibiotics that inhibit prodn. or activity of MshB and thereby reduce the prodn. of ***mycothiol*** and the virulence of the infecting bacteria.

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:435230 CAPLUS
DN 135:57858
TI Bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification
IN ***Newton, Gerald L.*** ; Av-gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2001042422 A2 20010614 WO 2000-US33232 20001207
WO 2001042422 A3 20020110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001020702 A5 20010618 AU 2001-20702 20001207
PRAI US 1999-169503P A2 19991207
WO 2000-US33232 W 20001207
AB The present invention provides a family of bacterial acyl glucosaminyl inositol amidases with amidase activity against S-conjugate amides, particularly ***mycothiol*** -derived S-conjugate amides. The invention amidases are characterized by a highly conserved 20 amino acid N-terminal region and four highly conserved histidine-contg. regions and by having amidase activity, particularly amide hydrolase activity. Purifn., characterization and sequences of ***mycothiol*** S-conjugate amidases of ***Mycobacterium*** smegmatis mc2 155 and M. tuberculosis H37Rv (Rv1082) are disclosed. The invention further provides methods for using the invention amidases in drug screening assays to det. compds. with antibiotic activity or compds. that inhibit activity or prodn. of endogenous acyl glucosaminylinositol amidase in bacteria. The invention further provides methods for detoxifying a toxic substance by contacting the toxic substance with an invention amidase, for example, by expression of the amidase under environmental conditions in a bacterium.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:288460 CAPLUS
DN 135:31474
TI Novel bromotyrosine alkaloids: Inhibitors of ***mycothiol*** S-conjugate amidase
AU Nicholas, Gillian M.; ***Newton, Gerald L.*** ; Fahey, Robert C.; Bewley, Carole A.
CS Laboratory of Bioorganic Chemistry, NIDDK National Institutes of Health, Bethesda, MD, 20892-0820, USA
SO Organic Letters (2001), 3(10), 1543-1545
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
AB The novel alkaloids (I) and (II) were isolated from an Australian non-verongid sponge, Oceanapia sp. Compd. I contains an unprecedented imidazolyl-quinolinone substructure attached to a bromotyrosine-derived spiro-isoxazoline. Three other known alkaloids were isolated in addn. to I and II and together represent the first examples of inhibitors of a new ***mycobacterial*** enzyme ***mycothiol*** S-conjugate amidase (MCA).
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

1
AN 2000:439612 BIOSIS
DN PREV200000439612
TI A novel ***mycothiol*** -dependent detoxification pathway in ***mycobacteria*** involving ***mycothiol*** S-conjugate amidase.
AU ***Newton, Gerald L.*** ; Av-Gay, Yossef; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093 USA
SO Biochemistry, (September 5, 2000) Vol. 39, No. 35, pp. 10739-10746. print. ISSN: 0006-2960.
DT Article
LA English
SL English
AB ***Mycothiol*** , 1-D-myo-inosityl-2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (MSH), is composed of N-acetylcysteine (AcCys) amide linked to 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (GlcN-Ins) and is the major thiol produced by most actinomycetes. When ***Mycobacterium*** smegmatis was treated with the alkylating agent monobromobimane (mBBr), the cellular ***mycothiol*** was converted to its bimane derivative (MSmB). The latter was rapidly cleaved to produce GlcN-Ins and the bimane derivative of N-acetylcysteine (AcCySmB), a mercapturic acid that was rapidly exported from the cells into the medium. The other product of cleavage, GlcN-Ins, was retained in the cell and utilized in the resynthesis of ***mycothiol*** . The ***mycothiol*** S-conjugate amidase (amidase) responsible for cleaving MSmB was purified to homogeneity from M. smegmatis. A value of Km = 95 +- 8 muM and a value of kcat = 8 s-1 was determined for the amidase with MSmB as substrate. Activity with 100 muM ***mycothiol*** or with the monobromobimane derivative of 1-D-myo-inosityl-2-(L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (CySmB-GlcN-Ins) or of 2-(N-acetyl-L-cysteinyl)amido-2-deoxy-(alpha,beta)-D-glucopyranoside (AcCySmB-GlcN) was at least 103 lower than with 100 muM MSmB, demonstrating that the amidase is highly specific for S-conjugates of ***mycothiol*** . Conjugates of ***mycothiol*** with the antibiotic cerulenin, N-ethylmaleimide, 3-(N-maleimidopropionyl)-biocytin, and 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin also exhibited significant activity. The sequence of the amino-terminal 20 residues was determined, and an open reading frame (Rv1082) coding for 288 residues having an identical predicted amino-terminal amino acid sequence was identified in the ***Mycobacterium*** tuberculosis genome. The Rv1082 gene (mca) from M. tuberculosis was cloned and expressed in Escherichia coli, and the expressed protein was shown to have substrate specificity similar to the amidase from M. smegmatis. These results indicate that ***mycothiol*** and ***mycothiol*** S-conjugate amidase play an important role in the detoxification of alkylating agents and antibiotics.

L4 ANSWER 5 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:313790 BIOSIS
DN PREV200100313790
TI N-acetyl-1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside deacetylase (MshB) is a key enzyme in ***mycothiol*** biosynthesis.
AU ***Newton, Gerald L.*** ; Av-Gay, Yossef; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506: rcfahey@ucsd.edu USA

SO Journal of Bacteriology, (December, 2000) Vol. 182, No. 24, pp. 6958-6963.
print.
ISSN: 0021-9193.
DT Article
LA English
SL English
AB ***Mycothiol*** is a novel thiol produced only by actinomycetes and is the major low-molecular-weight thiol in ***mycobacteria*** . ***Mycothiol*** was previously shown to be synthesized from 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside by ligation with cysteine followed by acetylation. A novel ***mycothiol*** -dependent detoxification enzyme, ***mycothiol*** conjugate amidase, was recently identified in ***Mycobacterium*** smegmatis and shown to have a homolog, Rv1082, in ***Mycobacterium*** tuberculosis. In the present study we found that a protein encoded by the M. tuberculosis open reading frame Rv1170, a homolog of Rv1082, possesses weak ***mycothiol*** conjugate amidase activity but shows substantial deacetylation activity with 1-D-myo-inosityl-2-acetamido-2-deoxy-alpha-D-glucopyranoside (GlcNAc-Ins), a hypothetical ***mycothiol*** biosynthetic precursor. The availability of this protein enabled us to develop an assay for GlcNAc-Ins, which was used to demonstrate that GlcNAc-Ins is present in M. smegmatis at a level about twice that of ***mycothiol*** . It was shown that GlcNAc-Ins is absent in ***mycothiol*** -deficient mutant strain 49 of M. smegmatis and that this strain can concentrate GlcNAc-Ins from the medium and convert it to ***mycothiol*** . This demonstrates that GlcNAc-Ins is a key intermediate in the pathway of ***mycothiol*** biosynthesis. Assignment of Rv1170 as the gene coding the deacetylase in the M. tuberculosis genome represents the first identification of a gene of the ***mycothiol*** biosynthesis pathway. The presence of a large cellular pool of substrate for this enzyme suggests that it may be important in regulating ***mycothiol*** biosynthesis.

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS
DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of ***mycothiol*** and precursors thereof
IN Fahey, Robert C.; ***Newton, Gerald L.*** ; Unson, Maria Margarita D.; Davis, Charles E.; Angerberg, Sara J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921580	A1	19990506	WO 1998-US22577	19981023

PI WO 9921580 A1 19990506 WO 1998-US22577 19981023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9911988 A1 19990517 AU 1999-11988 19981023
PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting ***mycothiol*** or precursor thereof. An antibody is provided which binds to ***mycothiol*** or a ***mycothiol*** precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of ***mycothiol*** or a precursor thereof. A method is provided for detecting ***mycothiol*** or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of ***mycothiol*** or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1999:310093 BIOSIS
DN PREV199900310093
TI Improved methods for immunoassay of ***mycothiol*** .
AU Unson, Mia D.; ***Newton, Gerald L.*** ; Arnold, Karen F.; Davis, Charles E.; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506 USA
SO Journal of Clinical Microbiology, (July, 1999) Vol. 37, No. 7, pp. 2153-2157.
ISSN: 0095-1137.
DT Article
LA English
SL English
AB Improved enzyme-linked immunosorbent assay (ELISA) methods have been developed for the determination of femtomole amounts of ***mycothiol*** (MSH), the main low-molecular-weight thiol in ***mycobacteria*** . The immunoassays utilize an affinity-purified rabbit polyclonal antibody that is highly specific for the pseudodisaccharide moiety of MSH. MSH was first biotinylated by the thiol-specific reagent 3-(N-maleimidopropionyl)biocytin. The MSH-biotin adduct was then captured with immobilized avidin and detected with anti-MSH antibody (biotin-capture ELISA) or was captured with immobilized anti-MSH antibody and detected with alkaline phosphatase-labelled avidin (MSH-capture ELISA). The MSH-capture ELISA was the most sensitive method, measuring as little as 0.3 fmol of MSH. Methods for biotinylating MSH directly from ***Mycobacterium*** spp. are described. The MSH-capture ELISA was tested for the detection of M. avium seeded in human urine or cerebrospinal fluid samples and for screening mutant M. smegmatis strains to detect MSH production.

L4 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 1999:148924 BIOSIS
DN PREV199900148924
TI Characterization of ***Mycobacterium*** smegmatis mutants defective in 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside and

mycothiol biosynthesis.

AU ***Newton, Gerald L.*** ; Unson, Mia D.; Anderberg, Sara J.; Aguilera, Joseph A.; Oh, Nancy N.; Delcardayre, Stephen B.; Av-Gay, Yossef; Fahey, Robert C. (1)

CS (1) Dep. Chem. Biochemistry, Univ. California, San Diego, La Jolla, CA 92093 USA

SO Biochemical and Biophysical Research Communications, (Feb. 16, 1999) Vol. 255, No. 2, pp. 239-244.
ISSN: 0006-291X.

DT Article

LA English

AB ***Mycothiol*** (MSH) is the major low molecular weight thiol in ***mycobacteria*** . Two chemical mutants with low MSH and one with no MSH (strain 49) were produced in ***Mycobacterium*** smegmatis mc2155 to assess the role of MSH in ***mycobacteria*** . Strain 49 was shown to not produce 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (GlcN-Ins), an intermediate in MSH biosynthesis. Relative to the parent strain, mutant 49 formed colonies more slowly on solid media and was more sensitive to H2O2, and rifampin, but less sensitive to isoniazid. Complementation of mutant 49 with DNA from M. tuberculosis H37Rv partially restored production of GlcN-Ins and MSH, and resistance to H2O2, but largely restored colony growth rate and sensitivity to rifampin and isoniazid. The results indicate that MSH and GlcN-Ins are not essential for in vitro survival of ***mycobacteria*** but may play significant roles in determining the sensitivity of ***mycobacteria*** to environmental toxins.

L4 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5

AN 1999:5037 BIOSIS

DN PREV199900005037

TI ***Mycothiol*** biosynthesis and metabolism: Cellular levels of potential intermediates in the biosynthesis and degradation of ***mycothiol*** in ***Mycobacterium*** smegmatis.

AU Anderberg, Sara J.; ***Newton, Gerald L.*** ; Fahey, Robert C. (1)

CS (1) Dep. Chem. Biochem., Univ. Calif. at San Diego, La Jolla, CA 92093-0506 USA

SO Journal of Biological Chemistry, (Nov. 13, 1998) Vol. 273, No. 46, pp. 30391-30397.
ISSN: 0021-9258.

DT Article

LA English

AB ***Mycothiol*** (MSH; 1-D-myo-inosityl-2-(N-acetyl-L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (AcCys-GlcN-Ins)) is a novel thiol produced at millimolar levels by ***mycobacteria*** and other actinomycetes that do not make glutathione. We developed methods to determine the major components of MSH (AcCys, Cys-GlcN, AcCys-GlcN, Cys-GlcN-Ins, GlcN-Ins) in cell extracts. ***Mycobacterium*** smegmatis was shown to produce measurable levels (nmol/g of residual dry weight) of AcCys (apprx30), Cys-GlcN-Ins (apprx8), and GlcN-Ins (apprx100) but not Cys-GlcN (<3) or AcCys-GlcN (<80) during exponential growth in Middlebrook 7H9 medium. The level of GlcN-Ins declined 10-fold in stationary phase and apprx5-fold in 7H9 medium lacking glucose. Incubation in 10 mM AcCys produced 50- and 1000-fold increases in cellular Cys and AcCys levels, respectively, a 10-fold decrease in GlcN-Ins and a transient 3-fold increase in

Cys-GlcN-Ins. These results exclude Cys-GlcN and AcCys-GlcN as intermediates in MSH biosynthesis and implicate GlcN-Ins and Cys-GlcN-Ins as key intermediates. Assay of GlcN-Ins/ATP-dependent ligase activity with Cys and AcCys as substrates revealed that Cys was at least an order of magnitude better substrate. Based on the cellular measurements, MSH biosynthesis involves assembly of GlcN-Ins, ligation with Cys to produce Cys-GlcN-Ins, and acetylation of the latter to produce MSH.

L4 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 1998:386859 BIOSIS
DN PREV199800386859
TI An immunoassay for the detection and quantitative determination of ***mycothiol*** .
AU Unson, Mia D.; ***Newton, Gerald L.*** ; Davis, Charles; Fahey, Robert C. (1)
CS (1) Dep. Chem. and Biochem., Univ. Calif., San Diego, La Jolla, CA 92093 USA
SO Journal of Immunological Methods, (May 1, 1998) Vol. 214, No. 1-2, pp. 29-39.
ISSN: 0022-1759.
DT Article
LA English
AB ***Mycothiol*** (MSH) is a glycosylated derivative of V-acetylcysteine that may have antioxidant functions in ***mycobacteria*** and other actinomycetes. To develop a highly specific assay for MSH, we capitalized on the selective binding of thiols to a maleimide residue linked to bovine serum albumin and employed affinity-purified polyclonal antibody and an enzyme-linked secondary antibody for detection. The assay was shown to be specific and to detect MSH at levels as low as 0.1 pmol when conducted in the form of a microtiter plate-based ELISA. A similar, nitrocellulose membrane-based immunoassay was shown to be useful for qualitative detection of MSH-producing bacterial colonies.

L4 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
AN 1996:232911 BIOSIS
DN PREV199698797040
TI Distribution of thiols in microorganisms: ***Mycothiol*** is a major thiol in most actinomycetes.
AU ***Newton, Gerald L.*** ; Arnold, Karen; Price, Mitchel S.; Sherrill, Christopher; Delcardayre, Stephen B.; Aharonowitz, Yair; Cohen, Gerald; Davies, Julian; Fahey, Robert C. (1); Davis, Charles
CS (1) Dep. Chemistry, University California, San Diego, La Jolla, CA 92093-0506 USA
SO Journal of Bacteriology, (1996) Vol. 178, No. 7, pp. 1990-1995.
ISSN: 0021-9193.
DT Article
LA English
AB ***Mycothiol*** (2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranosyl-(1 fwdarw 1)-myo-inositol) (MSH) has recently been identified as a major thiol in a number of actinomycetes (S. Sakuda, Z.-Y. Zhou, and Y. Yamada, Biosci. Biotech. Biochem. 58:1347-1348, 1994; H. S. C. Spies and D. J. Steenkamp, Eur. J. Biochem. 224:203213, 1994; and G. L. Newton, C. A. Bewley, T. J. Dwyer, R. Horn, Y. Aharonowitz, G. Cohen, J.

Davies, D. J. Faulkner, and R. C. Fahey, Eur. J. Biochem. 230:821-825, 1995). Since this novel thiol is more resistant than glutathione to heavy-metal ion-catalyzed oxidation, it seems likely to be the antioxidant thiol used by aerobic gram-positive bacteria that do not produce glutathione (GSH). In the present study we sought to define the spectrum of organisms that produce MSH. GSH was absent in all actinomycetes and some of the other gram-positive bacteria studied. Surprisingly, the streptococci and enterococci contained GSH, and some strains appeared to synthesize it rather than import it from the growth medium. MSH was found at significant levels in most actinomycetes examined. Among the actinobacteria four Micrococcus species produced MSH, but MSH was not found in representatives of the Arthrobacter, Agromyces, or Actinomyces genera. Of the nocardioforms examined, Nocardia, Rhodococcus, and ***Mycobacteria*** spp. all produced MSH. In addition to the established production of MSH by streptomycetes, we found that Micromonospora, Actinomadura, and Nocardiopsis spp. also synthesized MSH. ***Mycothiol*** production was not detected in Propionibacterium acnes or in representative species of the Listeria, Staphylococcus, Streptococcus, Enterococcus, Bacillus, and Clostridium genera. Examination of representatives of the cyanobacteria, purple bacteria, and spirochetes also gave negative results, as did tests of rat liver, bonito, Candida albicans, Neurospora crassa, and spinach leaves. The results, which indicate that MSH production is restricted to the actinomycetes, could have significant implications for the detection and treatment of infections with actinomycetes, especially those caused by ***mycobacteria*** .

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1995:630956 CAPLUS
DN 124:140470
TI The structure of U17 isolated from Streptomyces clavuligerus and its properties as an antioxidant thiol
AU ***Newton, Gerald L.*** ; Bewley, Carole A.; Dwyer, Tammy J.; Horn, Ronda; Aharonowitz, Yair; Cohen, Gerald; Davies, Julian; Faulkner, D. John; Fahey, Robert C.
CS Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506, USA
SO Eur. J. Biochem. (1995), 230(2), 821-5
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB The predominant low-mol.-mass thiol produced by streptomycetes is a cysteine deriv. previously designated as U17. In this study the elucidation of the structure of the monobromobimane deriv. of U17 (I) is reported, which establishes the structure of U17 as 2-(N-acetylcysteinyl)amido-2-deoxy-.alpha.-D-glucopyranosyl-myo-inositol. The presence of the N-acetylcysteine moiety was indicated by formation of N-acetylcysteine-monobromobimane during acid hydrolysis of I. Complete hydrolysis of I released 1 mol glucosamine/mol cysteine as detd. by carbohydrate and amino acid anal. High-resoln. mass spectral anal. gave a precise mass consistent with the mol. formula C27H40N4O14S. Anal. of 13C-NMR, 1-dimensional 1H-NMR and 2-dimensional NMR expts. identified the remaining C6H12O6 moiety as myo-inositol, confirmed the presence of N-acetyl-cysteine and glucosamine, and established the connectivity of the components. Two chem. properties of this novel thiol, which is equated to

mycothiol from ***Mycobacterium*** bovis, make it suitable as an intracellular storage form of cysteine and as an antioxidant thiol. First, it undergoes heavy-metal-ion catalyzed autoxidn. at a rate dramatically lower than that for cysteine and markedly lower than that for glutathione or N-acetylcysteine. Secondly, the .alpha.-(1.fwdarw.1) glycosidic link between glucosamine and myo-inositol is resistant to acid hydrolysis, hydrolyzing at a rate comparable to that of the 2 amide bonds in the mol.

=> e unson maria margarita/au
E1 3 UNSON DENNIS/AU
E2 24 UNSON M D/AU
E3 0 --> UNSON MARIA MARGARITA/AU
E4 2 UNSON MARIA MARGARITA D/AU
E5 10 UNSON MIA D/AU
E6 1 UNSON MIGUEL R JR/AU
E7 1 UNSON RENE E/AU
E8 4 UNSORG B/AU
E9 1 UNSOY M S/AU
E10 1 UNSPENSKII Y A/AU
E11 1 UNSPENSKII YU A/AU
E12 1 UNSPRUNG H/AU

=> s e4
L5 2 "UNSON MARIA MARGARITA D"/AU

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS
DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of mycothiol and precursors thereof
IN Fahey, Robert C.; Newton, Gerald L.; ***Unson, Maria Margarita D.*** ; Davis, Charles E.; Angerberg, Sara J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921580	A1	19990506	WO 1998-US22577	19981023

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9911988 A1 19990517 AU 1999-11988 19981023
PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting mycothiol or precursor thereof. An antibody is provided which binds to mycothiol or a mycothiol precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of mycothiol or a precursor thereof. A method is provided for detecting mycothiol or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of mycothiol or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1994:431558 CAPLUS
DN 121:31558
TI Chemical and biological studies of the symbiosis between a marine sponge and a cyanobacterium
AU ***Unson, Maria Margarita D.***
CS Univ. California, San Diego, CA, USA
SO (1993) 197 pp. Avail.: Univ. Microfilms Int., Order No. DA9410145
From: Diss. Abstr. Int. B, 1994, 54(11), 5676-7
DT Dissertation
LA English
AB Unavailable

=> e davis charles e/au
E1 2 DAVIS CHARLES CAVENDER/AU
E2 2 DAVIS CHARLES D/AU
E3 58 --> DAVIS CHARLES E/AU
E4 2 DAVIS CHARLES E JR/AU
E5 2 DAVIS CHARLES E S/AU
E6 1 DAVIS CHARLES EARNEST/AU
E7 4 DAVIS CHARLES F/AU
E8 2 DAVIS CHARLES F JR/AU
E9 1 DAVIS CHARLES FREEMAN JR/AU
E10 7 DAVIS CHARLES G/AU
E11 1 DAVIS CHARLES GARY/AU
E12 21 DAVIS CHARLES H/AU

=> s e3-e6 and myco?
L6 7 ("DAVIS CHARLES E"/AU OR "DAVIS CHARLES E JR"/AU OR "DAVIS CHARLES E S"/AU OR "DAVIS CHARLES EARNEST"/AU) AND MYCO?

=> dup rem l
ENTER L# LIST OR (END):l6
PROCESSING COMPLETED FOR L6
L7 6 DUP REM L6 L (1 DUPLICATE REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:169261 BIOSIS
DN PREV200000169261
TI Nosocomial transmission of ***Mycobacterium*** bovis bacille Calmette-Guerin to children receiving cancer therapy and to their health care providers.
AU Waecker, Norman J., Jr. (1); Stefanova, Rossina; Cave, M. Donald; ***Davis, Charles E.*** ; Dankner, Wayne M.
CS (1) Clinical Investigation Department, Naval Medical Center, 34800 Bob Wilson Drive, San Diego, CA, 92134-5000 USA
SO Clinical Infectious Diseases., (Feb., 2000) Vol. 30, No. 2, pp. 356-362. ISSN: 1058-4838.
DT Article
LA English
SL English
AB A previous report of nosocomial infection due to ***Mycobacterium*** bovis bacille Calmette-Guerin (BCG) implicated contamination of chemotherapy solutions reconstituted under the same biosafety hood as BCG vaccine used for bladder cancer therapy. We report 3 similar BCG infections in children and describe evidence of respiratory transmission to health care workers (HCWs) from 1 patient. These children were receiving chemotherapy for leukemia when they presented with active tuberculosis. Each isolate was identified biochemically and by both gas-liquid chromatography and major polymorphic tandem repeat-polymerase chain reaction. Pulsed-field gel electrophoresis showed that 2 isolates were identical strains and identical to the Tice and Connaught strains licensed in the United States for bladder chemotherapy. The third isolate differed by a single fragment after DraI restriction. One patient with heavily positive sputum exposed numerous HCWs. Of 41 HCWs, 2 (5%) converted their purified protein derivatives (PPD) skin test. These data underscore the risk of nosocomial BCG transmission by contamination of chemotherapy solutions and demonstrate the potential for transmission to HCWs from patients with active pulmonary disease.

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS
DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of ***mycothiol*** and precursors thereof
IN Fahey, Robert C.; Newton, Gerald L.; Unson, Maria Margarita D.; ***Davis, Charles E.*** ; Angerberg, Sara J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921580	A1	19990506	WO 1998-US22577	19981023

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9911988 A1 19990517 AU 1999-11988 19981023
PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting ***mycothiol*** or precursor thereof. An antibody is provided which binds to ***mycothiol*** or a ***mycothiol*** precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of ***mycothiol*** or a precursor thereof. A method is provided for detecting ***mycothiol*** or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of ***mycothiol*** or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1999:310093 BIOSIS
DN PREV199900310093
TI Improved methods for immunoassay of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Arnold, Karen F.; ***Davis, Charles*** *** E.*** ; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506 USA
SO Journal of Clinical Microbiology, (July, 1999) Vol. 37, No. 7, pp. 2153-2157.
ISSN: 0095-1137.
DT Article
LA English
SL English
AB Improved enzyme-linked immunosorbent assay (ELISA) methods have been developed for the determination of femtomole amounts of ***mycothiol*** (MSH), the main low-molecular-weight thiol in ***mycobacteria*** . The immunoassays utilize an affinity-purified rabbit polyclonal antibody that is highly specific for the pseudodisaccharide moiety of MSH. MSH was first biotinylated by the thiol-specific reagent 3-(N-maleimidopropionyl)biocytin. The MSH-biotin adduct was then captured with immobilized avidin and detected with anti-MSH antibody (biotin-capture ELISA) or was captured with immobilized anti-MSH antibody and detected with alkaline phosphatase-labelled avidin (MSH-capture ELISA). The MSH-capture ELISA was the most sensitive method, measuring as little as 0.3 fmol of MSH. Methods for biotinylating MSH directly from ***Mycobacterium*** spp. are described. The MSH-capture ELISA was tested for the detection of M. avium seeded in human urine or cerebrospinal fluid samples and for screening mutant M. smegmatis strains to detect MSH production.

L7 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:172725 BIOSIS
DN PREV199344080325
TI ***Mycobacterium*** bovis infections in San Diego: A clinicoepidemiologic study of 73 patients and a historical review of a

forgotten pathogen.
AU Dankner, Wayne M.; Waecker, Norman J.; Essey, Mitchell A.; Moser, Kathleen; Thompson, Muriel; ***Davis, Charles E. (1)***
CS (1) UCSD Medical Center 8416, 225 Dickinson St., San Diego, CA 92103 USA
SO Medicine (Baltimore), (1993) Vol. 72, No. 1, pp. 11-37.
ISSN: 0025-7974.
DT General Review
LA English

L7 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:146976 BIOSIS
DN PREV199395079776
TI Basic epidemiology of tuberculosis in Peru: A prevalence study of tuberculin sensitivity in a pueblo joven.
AU Getchell, William S.; ***Davis, Charles E. (1)*** ; Gilman, Josephine; Urueta, Guillermo; Ruiz-Huidobro, Ernesto; Gilman, Robert H.
CS (1) Dep. Pathol., Univ. Calif. San Diego Med. Cent. 8416, 225 Dickinson St., San Diego, Calif. 92103-8416
SO American Journal of Tropical Medicine and Hygiene, (1992) Vol. 47, No. 6, pp. 721-729.
ISSN: 0002-9637.
DT Article
LA English
AB Tuberculosis continues to cause significant morbidity and mortality in developing nations. As a first step in defining the magnitude of the problem in Peru, we determined the prevalence of tuberculin sensitivity in an age-stratified, community-based population on the outskirts of Lima in December 1990. The overall prevalence of 10 mm or more induration in 368 individuals was 34%. When stratified by age, the prevalence was 12% in the 0-1-year-old group, 18% in the 2-4-year-old group, 24% in the 5-14-year-old group, 60% in the 15-24-year-old group, and 68% in the ltoreq 25-year-old group. Vaccination with bacillus Calmette-Guerin (87% of the study population) caused significant increases in weak (5-9 mm) reactions to purified protein derivative, but did not cause strong (10 mm or more) reactions. The prevalence of tuberculous infection in this population is higher than that previously reported in Peru and in most other high-risk populations. Unfortunately, the current political and economic situation in Peru makes if difficult to implement public health measures to prevent infection and progression of infection to disease.

L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 1988:420136 CAPLUS
DN 109:20136
TI In vitro susceptibility of ***Mycobacterium*** avium complex to antibacterial agents
AU ***Davis, Charles E., Jr.*** ; Carpenter, John L.; Trevino, Sylvia; Koch, John; Ognibene, Andre J.
CS Dep. Med., Brooke Army Med. Cent., Fort Sam Houston, TX, USA
SO Diagn. Microbiol. Infect. Dis. (1987), 8(3), 149-55
CODEN: DMIDDZ; ISSN: 0732-8893
DT Journal
LA English
AB In vitro agar diln. susceptibility studies were performed by utilizing 20 isolates (24 against rifamycin) of the M. avium complex against several antimicrobial agents not routinely tested in the ***mycobacteriol*** .

lab. Thirteen strains were susceptible to gentamicin at 4 .mu.g/mL, 20 to amikacin at 8 .mu.g/mL, 18 to streptomycin at 8 .mu.g/mL, 20 to kanamycin at 8 .mu.g/mL, 20 to trimethoprim/sulfamethoxazole at 2 .mu.g/mL, 12 to sulfisoxazole at 10 .mu.g/mL, and 14 to rifabutin at 1 .mu.g/mL. No activity was found with penicillin G, cephapirin, moxalactam, vancomycin, clindamycin, erythromycin, trimethoprim, or minocycline. The data suggests a potential use of trimethoprim/sulfamethoxazole, amikacin, gentamicin, and kanamycin in the treatment of infections caused by this group of organisms.

=> e angerberg sara j/au
E1 119 ANGERBAUER ROLF/AU
E2 1 ANGERBAUER ROSE H/AU
E3 1 --> ANGERBERG SARA J/AU
E4 1 ANGERBJOEN A/AU
E5 20 ANGERBJOERN A/AU
E6 55 ANGERBJORN A/AU
E7 16 ANGERBJORN ANDERS/AU
E8 1 ANGERBRANDT WILLIAM/AU
E9 1 ANGERE J/AU
E10 1 ANGEREN SIGRID/AU
E11 49 ANGERER A/AU
E12 1 ANGERER ALBIN/AU

=> s e3
L8 1 "ANGERBERG SARA J"/AU

=> d bib ab

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS
DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of mycothiol and precursors thereof
IN Fahey, Robert C.; Newton, Gerald L.; Unson, Maria Margarita D.; Davis, Charles E.; ***Angerberg, Sara J.***
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921580	A1	19990506	WO 1998-US22577	19981023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911988	A1	19990517	AU 1999-11988	19981023

PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting mycothiol or precursor thereof. An antibody is provided which binds to mycothiol or a mycothiol precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of mycothiol or a precursor thereof. A method is provided for detecting mycothiol or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of mycothiol or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s mycothiol?
L9 138 MYCOTHIOL?

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 38 DUP REM L9 (100 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 38 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 38 USPATFULL
AN 2002:57833 USPATFULL
TI Manipulating nitrosative stress to upregulate nitrosative stress defenses
IN Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States
PA Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin, Milwaukee, WI, United States (U.S. corporation)
PI US 6359004 B1 20020319
AI US 2000-690989 20001018 (9)
RLI Continuation of Ser. No. US 1999-361167, filed on 27 Jul 1999, now patented, Pat. No. US 6180824 Division of Ser. No. US 1997-852490, filed on 7 May 1997, now patented, Pat. No. US 6057367
PRAI US 1996-25819P 19960830 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Weddington, Kevin E.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3105
AB Mammals are treated for infections or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and

the S-alkyl- contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

L10 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2002 ACS
AN 2002:182733 CAPLUS
TI Total Synthesis and Proof of Structure of ***Mycothiol*** Bimane
AU Nicholas, Gillian M.; Kovac, Pavol; Bewley, Carole A.
CS Laboratories of Bioorganic Chemistry and Medicinal Chemistry, NIDDK National Institutes of Health, Bethesda, MD, 20892-0820, USA
SO Journal of the American Chemical Society (2002), 124(14), 3492-3493 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB ***Mycothiol*** is a low-mol. wt. thiol produced by actinomycetes that serves to protect these organisms from oxidative stress and alkylating agents. We report the total synthesis of ***mycothiol*** bimane (1) which is a commonly isolated deriv. of ***mycothiol*** . The synthesis confirms the original structure assignment and unambiguously establishes the abs. stereochem. of ***mycothiol*** to be 1-D-myo-inosityl 2-deoxy-2-(N-acetamido-L-cysteinamido)-.alpha.-D-glucopyranoside.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
AN 2002:106189 CAPLUS
TI Synthesis of ***mycothiol*** , 1D-1-O-(2-[N-acetyl-l-cysteinyl]amino-2-deoxy-.alpha.-d-glucopyranosyl)-myo-inositol, principal low molecular mass thiol in the actinomycetes
AU Jardine, M. Anwar; Spies, Hendrik S. C.; Nkambule, Comfort M.; Gammon, David W.; Steenkamp, Daniel J.
CS Department of Chemical Pathology, University of Cape Town Medical School, Observatory, 7925, S. Afr.
SO Bioorganic & Medicinal Chemistry (2002), 10(4), 875-881 CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB Members of the actinomycetes produce 1D-1-O-(2-[N-acetyl-l-cysteinyl]amino-2-deoxy-.alpha.-d-glucopyranosyl)-myo-inositol or ***mycothiol*** 1 as principal low mol. mass thiol. Chem. synthesis of a biosynthetic precursor of ***mycothiol*** , the pseudodisaccharide 1D-1-O-(2-amino-2-deoxy-.alpha.-d-glucopyranosyl)-myo-inositol 13 was achieved by the following steps: (1) Enantioselective synthesis gave the glycosyl acceptors (-)-2,3,4,5,6-penta-O-acetyl-d-myo-inositol D-7 and the corresponding l-isomer L-7. (2) Condensation of D-7 and L-7 with the glycosyl donor 3,4,6-tri-O-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-

.alpha.-d-glucopyranosylbromide afforded the corresponding .alpha. and .beta. anomeric products, which could be resolved by silica gel chromatog. (3) Deprotection of these by hydrolysis using an anion exchange resin gave 1D- and 1L-1-O-(2-amino-2-deoxy-.alpha.-d-glucopyranosyl)-myo-inositol 13 and 15 and the corresponding .beta.-coupled anomers 14 and 16. Only 13, and to a much lesser extent 15, were used by enzymes present in an ammonium sulfate fraction of a cellfree ext. of Mycobacterium smegmatis for the enzymic synthesis of ***mycothiol*** . In the absence of acetyl-SCoA, the immediate biosynthetic precursor of 1, desacetylmycothiol, was the major product.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 38 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 2002:207382 SCISEARCH
GA The Genuine Article (R) Number: 525FM
TI Functional genomics reveals the sole sulphate transporter of the Mycobacterium tuberculosis complex and its relevance to the acquisition of sulphur in vivo
AU Wooff E; Michell S L; Gordon S V; Chambers M A; Bardarov S; Jacobs W R; Hewinson R G; Wheeler P R (Reprint)
CS Vet Labs Agcy Weybridge, TB Res Grp, Surrey, England (Reprint); Albert Einstein Coll Med, Howard Hughes Med Inst, Bronx, NY 10467 USA
CYA England; USA
SO MOLECULAR MICROBIOLOGY, (FEB 2002) Vol. 43, No. 3, pp. 653-663.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0950-382X.
DT Article; Journal
LA English
REC Reference Count: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Sulphur is essential for some of the most vital biological activities such as translation initiation and redox maintenance, and genes involved in sulphur metabolism have been implicated in virulence. Mycobacterium tuberculosis has three predicted genes for the prototrophic acquisition of sulphur as sulphate: cysA, part of an ABC transporter, and cysA2 and A3, SseC sulphotransferases. Screening for amino acid auxotrophs of Mycobacterium bovis BCG, obtained by transposon mutagenesis, was used to select methionine auxotrophs requiring a sulphur-containing amino acid for growth. We have characterized one of these auxotrophs as being disrupted in cysA. Both the cysA mutant and a previously identified mutant in an upstream gene, sub1, were functionally characterized as being completely unable to take up sulphate. Complementation of the cysA mutant with the wild-type gene from M. tuberculosis restored prototrophy and the ability to take up sulphate with the functional characteristics of an ABC transporter. Hence, it appears that this is the sole locus encoding inorganic sulphur transport in the M. tuberculosis complex.

L10 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2002 ACS
AN 2001:923972 CAPLUS
DN 136:66199
TI Mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with analytical and antimicrobial inhibitor design uses

IN Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, San Diego, USA; University of British Columbia
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096529	A2	20011220	WO 2001-US19091	20010614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-211612P P 20000614
AB The present invention provides a family of bacterial acetylglucosaminylinositol deacetylases (MshB) with deacetylase activity against acylglucosaminylinositol and which play a key role in ***mycothiol*** biosynthesis. The invention deacetylases are characterized by a conserved 100 amino acid N-terminal region and 3 highly conserved histidine-contg. regions and by having deacetylase activity as well as amide hydrolase activity. The invention further provides methods for using the invention deacetylases in drug screening assays to det. compds. that inhibit activity. The invention provides for treatment of actinomycete infections in mammals using antibiotics that inhibit prodn. or activity of MshB and thereby reduce the prodn. of ***mycothiol*** and the virulence of the infecting bacteria.

L10 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2002 ACS
AN 2001:435230 CAPLUS
DN 135:57858
TI Bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification
IN Newton, Gerald L.; Av-gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042422	A2	20010614	WO 2000-US33232	20001207
WO 2001042422	A3	20020110		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001020702 A5 20010618 AU 2001-20702 20001207
PRAI US 1999-169503P A2 19991207
WO 2000-US33232 W 20001207
AB The present invention provides a family of bacterial acyl glucosaminyl inositol amidases with amidase activity against S-conjugate amides, particularly ***mycothiol*** -derived S-conjugate amides. The invention amidases are characterized by a highly conserved 20 amino acid N-terminal region and four highly conserved histidine-contg. regions and by having amidase activity, particularly amide hydrolase activity. Purifn., characterization and sequences of ***mycothiol*** S-conjugate amidases of Mycobacterium smegmatis mc2 155 and M. tuberculosis H37Rv (Rv1082) are disclosed. The invention further provides methods for using the invention amidases in drug screening assays to det. compds. with antibiotic activity or compds. that inhibit activity or prodn. of endogenous acyl glucosaminylinositol amidase in bacteria. The invention further provides methods for detoxifying a toxic substance by contacting the toxic substance with an invention amidase, for example, by expression of the amidase under environmental conditions in a bacterium.

L10 ANSWER 7 OF 38 USPATFULL
AN 2001:14679 USPATFULL
TI Manipulating nitrosative stress to kill pathologic microbes, pathologic helminths and pathologically, proliferating cells or to upregulate nitrosative stress defenses
IN Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States
PA Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin, Milwaukee, WI, United States (U.S. corporation)
PI US 6180824 B1 20010130
AI US 1999-361167 19990727 (9)
RLI Division of Ser. No. US 1997-852490, filed on 7 May 1997, now patented, Pat. No. US 6057367
PRAI US 1996-25819P 19960830 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Weddington, Kevin E.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammals are treated for infection or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and

the S-alkyl- contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

L10 ANSWER 8 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:201920 BIOSIS
DN PREV200200201920
TI Novel thiols of prokaryotes.
AU Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093: rcfahey@ucsd.edu USA
SO Ornston, L. Nicholas [Editor]; Balows, Albert [Editor]; Gottesman, Susan [Editor]. Annual Review of Microbiology, (2001) Vol. 55, pp. 333-356.
Annual Review of Microbiology. print.
Publisher: Annual Reviews 4139 El Camino Way, Palo Alto, CA, 94303-0139, USA.
ISSN: 0066-4227.
DT Book
LA English

L10 ANSWER 9 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:257195 BIOSIS
DN PREV200100257195
TI Mycobacterium tuberculosis mycothione reductase: pH dependence of the kinetic parameters and kinetic isotope effects.
AU Patel, Mehul P.; Blanchard, John S. (1)
CS (1) Department of Biochemistry, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY, 10461: blanchar@aecom.yu.edu USA
SO Biochemistry, (May 1, 2001) Vol. 40, No. 17, pp. 5119-5126. print.
ISSN: 0006-2960.
DT Article
LA English
SL English
AB The recent identification of the enzyme in Mycobacterium tuberculosis that catalyzes the NADPH-dependent reduction of the unique low molecular weight disulfide mycothione, mycothione reductase, has led us to examine the mechanism of catalysis in greater detail. The pH dependence of the kinetic parameters V and V/K for NADPH, NADH, and an active analogue of mycothione disulfide, des-myo-inositol mycothione disulfide, has been determined. An analysis of the pH profiles has allowed the tentative assignment of catalytically significant residues crucial to the mechanism of disulfide reduction, namely, the His444-Glu449 ion pair and Cys39. Solvent kinetic isotope effects were observed on V and V/KDIMSSM, yielding values of 1.7 +- 0.2 and 1.4 +- 0.2, respectively, but not on V/KNADPH. Proton inventory studies (V versus mole fraction of D2O) were linear, indicative of a single proton transfer in a solvent isotopically sensitive step. Steady-state primary deuterium kinetic isotope effects on V have been

determined using NADPH and NADH, yielding values of 1.27 +- 0.03 and 1.66 +- 0.14, respectively. The pre-steady-state primary deuterium kinetic isotope effect on enzyme reduction has values of 1.82 +- 0.04 and 1.59 +- 0.06 for NADPH and NADH, respectively. The steady-state primary deuterium kinetic isotope effect using NADH coincide with that obtained under single turnover conditions, suggesting the complete expression of the intrinsic primary kinetic isotope effect. Rapid reaction studies on the reductive half-reaction using NADPH and NADH yielded maximal rates of 129 +- 2 and 20 +- 1 s-1, respectively, while similar studies of the oxidation of the two-electron reduced enzyme by ***mycothiol*** disulfide yielded a maximum rate of 190 +- 10 s-1. These data suggest a unique flavoprotein disulfide mechanism in which the rate of the oxidative half-reaction is slightly faster than the rate of the reductive half-reaction.

L10 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
AN 2001:288460 CAPLUS
DN 135:31474
TI Novel bromotyrosine alkaloids: Inhibitors of ***mycothiol*** S-conjugate amidase
AU Nicholas, Gillian M.; Newton, Gerald L.; Fahey, Robert C.; Bewley, Carole A.
CS Laboratory of Bioorganic Chemistry, NIDDK National Institutes of Health, Bethesda, MD, 20892-0820, USA
SO Organic Letters (2001), 3(10), 1543-1545
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
AB The novel alkaloids (I) and (II) were isolated from an Australian non-verongid sponge, Oceanapia sp. Compd. I contains an unprecedented imidazolyl-quinolinone substructure attached to a bromotyrosine-derived spiro-isoxazoline. Three other known alkaloids were isolated in addn. to I and II and together represent the first examples of inhibitors of a new mycobacterial enzyme ***mycothiol*** S-conjugate amidase (MCA).
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2002:813 BIOSIS
DN PREV200200000813
TI Defining the disulphide stress response in Streptomyces coelicolor A3(2): Identification of the sigmaR regulon.
AU Paget, Mark S. B. (1); Molle, Virginie; Cohen, Gerald; Aharonowitz, Yair; Buttner, Mark J.
CS (1) School of Biological Sciences, University of Sussex, Brighton, BN1 9QG: M.Paget@sussex.ac.uk UK
SO Molecular Microbiology, (November, 2001) Vol. 42, No. 4, pp. 1007-1020. print.
ISSN: 0950-382X.
DT Article
LA English
AB In the Gram-positive, antibiotic-producing bacterium Streptomyces coelicolor A3(2), the thiol-disulphide status of the hyphae is controlled by a novel regulatory system consisting of a sigma factor, sigmaR, and its

cognate anti-sigma factor, RsrA. Oxidative stress induces intramolecular disulphide bond formation in RsrA, which causes it to lose affinity for sigmaR, thereby releasing sigmaR to activate transcription of the thioredoxin operon, trxBA. Here, we exploit a preliminary consensus sequence for sigmaR target promoters to identify 27 new sigmaR target genes and operons, thereby defining the global response to disulphide stress in this organism. Target genes related to thiol metabolism encode a second thioredoxin (TrxC), a glutaredoxin-like protein and enzymes involved in the biosynthesis of the low-molecular-weight thiol-containing compounds cysteine and molybdopterin. In addition, the level of the major actinomycete thiol buffer, ***mycothiol*** , was fourfold lower in a sigR null mutant, although no candidate ***mycothiol*** biosynthetic genes were identified among the sigmaR targets. Three sigmaR target genes encode ribosome-associated products (ribosomal subunit L31, ppGpp synthetase and tmRNA), suggesting that the translational machinery is modified by disulphide stress. The product of another sigmaR target gene was found to be a novel RNA polymerase-associated protein, RbpA, suggesting that the transcriptional machinery may also be modified in response to disulphide stress. We present DNA sequence evidence that many of the targets identified in S. coelicolor are also under the control of the sigmaR homologue in the actinomycete pathogen Mycobacterium tuberculosis.

L10 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
AN 2001:776059 CAPLUS
DN 136:34381
TI Novel thiols of prokaryotes
AU Fahey, Robert C.
CS Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093, USA
SO Annual Review of Microbiology (2001), 55, 333-356
CODEN: ARMIAZ; ISSN: 0066-4227
PB Annual Reviews Inc.
DT Journal; General Review
LA English
AB A review. Glutathione metab. is assocd. with oxygenic cyanobacteria and the oxygen-utilizing purple bacteria, but is absent in many other prokaryotes. This review focuses on novel thiols found in those bacteria lacking glutathione. Included are glutathione amide and its perthiol, produced by phototrophic purple sulfur bacteria and apparently involved in their sulfide metab. Among archaebacteria, coenzyme M (2-mercaptoethanesulfonic acid) and coenzyme B (7-mercaptoheptanoylthreonine phosphate) play central roles in the anaerobic prodn. of CH4 and assocd. energy conversion by methanogens, whereas the major thiol in the aerobic phototrophic halobacteria is .gamma.-glutamylcysteine. The highly aerobic actinomycetes produce ***mycothiol*** , a conjugate of N-acetylcysteine with a pseudodisaccharide of glucosamine and myo-inositol, AcCys-GlcN.alpha.(1 .fwdarw. 1)Ins, which appears to play an antioxidant role similar to glutathione. Ergothioneine, also produced by actinomycetes, remains a mystery despite many years of study. Available data on the biosynthesis and metab. of these and other novel thiols is summarized and key areas for addnl. study are identified.
RE.CNT 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001221109 EMBASE
TI Brave new world of post-genomics!.
AU Fairlamb A.H.
CS A.H. Fairlamb, Division of Biological Chemistry, Wellcome Trust Biocentre, University of Dundee, Dundee DD1 5EH, United Kingdom.
a.h.fairlamb@dundee.ac.uk
SO Trends in Parasitology, (2001) 17/6 (255-256).
Refs: 10
ISSN: 1471-4922 CODEN: TPRACT
PUI S 1471-4922(01)01977-8
CY United Kingdom
DT Journal; Conference Article
FS 004 Microbiology
037 Drug Literature Index
LA English

L10 ANSWER 14 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 2001:127195 BIOSIS
DN PREV200100127195
TI Characterization of the Mycobacterium tuberculosis H37Rv alkyl hydroperoxidase AhpC points to the importance of ionic interactions in oligomerization and activity.
AU Chauhan, Radha; Mande, Shekhar C. (1)
CS (1) Institute of Microbial Technology, Sector 39-A, Chandigarh, 160 036: shekhar@imtech.ernet.in India
SO Biochemical Journal, (15 February, 2001) Vol. 354, No. 1, pp. 209-215.
print.
ISSN: 0264-6021.
DT Article
LA English
SL English
AB An alkyl hydroperoxidase (AhpC) has been found frequently to be overexpressed in isoniazid-resistant strains of Mycobacterium tuberculosis. These strains have an inactivated katG gene encoding a catalase peroxidase, which might render mycobacteria susceptible to the toxic peroxide radicals, thus leading to the concomitant overexpression of the AhpC. Although the overexpressed AhpC in isoniazid-resistant strains of M. tuberculosis may not directly participate in isoniazid action, AhpC might still assist M. tuberculosis in combating oxidative damage in the absence of the catalase. Here we have attempted to characterize the AhpC protein biochemically and report its functional and oligomerization properties. The alkyl hydroperoxidase of M. tuberculosis is unique in many ways compared with its well-characterized homologues from enteric bacteria. We show that AhpC is a decameric protein, composed of five identical dimers held together by ionic interactions. Dimerization of individual subunits takes place through an intersubunit disulphide linkage. The ionic interactions play a significant role in enzymic activity of the AhpC protein. The UV absorption spectrum and three-dimensional model of AhpC suggest that interesting conformational changes may take place during oxidation and reduction of the intersubunit disulphide linkage. In the absence of the partner AhpF subunit in M. tuberculosis, the mycobacterial AhpC might use small-molecule reagents,

such as ***mycothiol*** , for completing its enzymic cycle.

L10 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
AN 2001:634894 CAPLUS
DN 135:368337
TI Cofactor diversity in biological oxidations: implications and applications
AU Duine, Johannis A.
CS Department of Microbiology and Enzymology, Technische Universiteit Delft, Schiedam, 3124 KE, Neth.
SO Chemical Record (2001), 1(1), 74-83
CODEN: CRHEAK; ISSN: 1527-8999
PB John Wiley & Sons, Inc.
DT Journal; General Review
LA English
AB A review, with refs. Until recently, it was generally believed that enzymic oxidn. and redn. requires the participation of either a nicotinamide (NAD(P)+) or a flavin (FAD, FMN), in agreement with the existence of NAD(P)/H-dependent dehydrogenases/reductases and flavoprotein dehydrogenases/reductases/oxidases. However, during the past 20 yr, the unraveling of the enzymol. of the oxidn. and redn. of C1-compds. by bacteria has led to the discovery of many new redox cofactors, some of them discussed here as they have a wider physiol. significance than just enabling enzymic C1-conversions to occur. A good example is the quinone cofactors, encompassing PQQ (2,7,9-tricarboxy-1H-pyrrolo[2,3-f]-quinoline-4,5-dione), TTQ (tryptophyl tryptophanquinone), TPQ (topaquinone), LTQ (lysyl topaquinone), and several others whose structures have still to be elucidated. Another example is ***mycothiol*** (1-O-(2'-[N-acetyl-L-cysteinyl]amido-2'-deoxy-.alpha.-D-glucopyranosyl)-D-myo-inosoirol), the counterpart of glutathione, once thought to be a universal coenzyme. Because these novel cofactors assist in reactions that can also be catalyzed by already known enzyme "classic cofactor" combinations, and first indications suggest that the chem. of the reactions is not unique, one may wonder about the evolutionary background for this cofactor diversity. However, as will be illustrated by examples, from a practical point of view the diversity is beneficial, as it has increased the arsenal of enzymes suitable for application.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 38 USPATFULL
AN 2000:54150 USPATFULL
TI Manipulating nitrosative stress to kill pathologic microbes, pathologic helminths and pathologically proliferating cells or to upregulate nitrosative stress defenses
IN Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States
PA Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin Research Foundation, Inc., Milwaukee, WI, United States (U.S. corporation)
PI US 6057367 20000502
AI US 1997-852490 19970507 (8)
PRAI US 1996-25819P 19960830 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Weddington, Kevin E.

CLMN Number of Claims: 66
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3415
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammals are treated for infections or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and the S-alkyl-contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

L10 ANSWER 17 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8
AN 2000:439612 BIOSIS
DN PREV200000439612
TI A novel ***mycothiol*** -dependent detoxification pathway in mycobacteria involving ***mycothiol*** S-conjugate amidase.
AU Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093 USA
SO Biochemistry, (September 5, 2000) Vol. 39, No. 35, pp. 10739-10746. print. ISSN: 0006-2960.
DT Article
LA English
SL English
AB ***Mycothiol*** , 1-D-myo-inosityl-2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (MSH), is composed of N-acetylcysteine (AcCys) amide linked to 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (GlcN-Ins) and is the major thiol produced by most actinomycetes. When Mycobacterium smegmatis was treated with the alkylating agent monobromobimane (mBBr), the cellular ***mycothiol*** was converted to its bimane derivative (MSmB). The latter was rapidly cleaved to produce GlcN-Ins and the bimane derivative of N-acetylcysteine (AcCySmB), a mercapturic acid that was rapidly exported from the cells into the medium. The other product of cleavage, GlcN-Ins, was retained in the cell and utilized in the resynthesis of ***mycothiol*** . The ***mycothiol*** S-conjugate amidase (amidase) responsible for cleaving MSmB was purified to homogeneity from M. smegmatis. A value of Km = 95 +- 8 muM and a value of kcat = 8 s-1 was determined for the amidase with MSmB as substrate. Activity with 100 muM ***mycothiol*** or with the monobromobimane derivative of 1-D-myo-inosityl-2-(L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (CySmB-GlcN-Ins) or of 2-(N-acetyl-L-cysteinyl)amido-2-

deoxy-(alpha,beta)-D-glucopyranoside (AcCySmB-GlcN) was at least 103 lower than with 100 muM MSmB, demonstrating that the amidase is highly specific for S-conjugates of ***mycothiol*** . Conjugates of ***mycothiol*** with the antibiotic cerulenin, N-ethylmaleimide, 3-(N-maleimidopropionyl)-biocytin, and 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin also exhibited significant activity. The sequence of the amino-terminal 20 residues was determined, and an open reading frame (Rv1082) coding for 288 residues having an identical predicted amino-terminal amino acid sequence was identified in the Mycobacterium tuberculosis genome. The Rv1082 gene (mca) from M. tuberculosis was cloned and expressed in Escherichia coli, and the expressed protein was shown to have substrate specificity similar to the amidase from M. smegmatis. These results indicate that ***mycothiol*** and ***mycothiol*** S-conjugate amidase play an important role in the detoxification of alkylating agents and antibiotics.

L10 ANSWER 18 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9

AN 2001:313790 BIOSIS

DN PREV200100313790

TI N-acetyl-1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside deacetylase (MshB) is a key enzyme in ***mycothiol*** biosynthesis.

AU Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C. (1)

CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506: rcfahey@ucsd.edu USA

SO Journal of Bacteriology, (December, 2000) Vol. 182, No. 24, pp. 6958-6963. print.
ISSN: 0021-9193.

DT Article

LA English

SL English

AB ***Mycothiol*** is a novel thiol produced only by actinomycetes and is the major low-molecular-weight thiol in mycobacteria. ***Mycothiol*** was previously shown to be synthesized from 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside by ligation with cysteine followed by acetylation. A novel ***mycothiol*** -dependent detoxification enzyme, ***mycothiol*** conjugate amidase, was recently identified in Mycobacterium smegmatis and shown to have a homolog, Rv1082, in Mycobacterium tuberculosis. In the present study we found that a protein encoded by the M. tuberculosis open reading frame Rv1170, a homolog of Rv1082, possesses weak ***mycothiol*** conjugate amidase activity but shows substantial deacetylation activity with 1-D-myo-inosityl-2-acetamido-2-deoxy-alpha-D-glucopyranoside (GlcNAc-Ins), a hypothetical ***mycothiol*** biosynthetic precursor. The availability of this protein enabled us to develop an assay for GlcNAc-Ins, which was used to demonstrate that GlcNAc-Ins is present in M. smegmatis at a level about twice that of ***mycothiol*** . It was shown that GlcNAc-Ins is absent in ***mycothiol*** -deficient mutant strain 49 of M. smegmatis and that this strain can concentrate GlcNAc-Ins from the medium and convert it to ***mycothiol*** . This demonstrates that GlcNAc-Ins is a key intermediate in the pathway of ***mycothiol*** biosynthesis. Assignment of Rv1170 as the gene coding the deacetylase in the M. tuberculosis genome represents the first identification of a gene of the ***mycothiol*** biosynthesis pathway. The presence of a large cellular pool of substrate for this enzyme suggests that it may be important in regulating ***mycothiol*** biosynthesis.

L10 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS
DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of ***mycothiol*** and precursors thereof
IN Fahey, Robert C.; Newton, Gerald L.; Unson, Maria Margarita D.; Davis, Charles E.; Angerberg, Sara J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921580	A1	19990506	WO 1998-US22577	19981023
AU 9911988	A1	19990517	AU 1999-11988	19981023

PI WO 9921580 A1 19990506 WO 1998-US22577 19981023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9911988 A1 19990517 AU 1999-11988 19981023
PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting ***mycothiol*** or precursor thereof. An antibody is provided which binds to ***mycothiol*** or a ***mycothiol*** precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of ***mycothiol*** or a precursor thereof. A method is provided for detecting ***mycothiol*** or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of ***mycothiol*** or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
AN 1999:310093 BIOSIS
DN PREV199900310093
TI Improved methods for immunoassay of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Arnold, Karen F.; Davis, Charles E.; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506 USA
SO Journal of Clinical Microbiology, (July, 1999) Vol. 37, No. 7, pp. 2153-2157.
ISSN: 0095-1137.
DT Article
LA English

SL English

AB Improved enzyme-linked immunosorbent assay (ELISA) methods have been developed for the determination of femtomole amounts of ***mycothiol*** (MSH), the main low-molecular-weight thiol in mycobacteria. The immunoassays utilize an affinity-purified rabbit polyclonal antibody that is highly specific for the pseudodisaccharide moiety of MSH. MSH was first biotinylated by the thiol-specific reagent 3-(N-maleimidopropionyl)biocytin. The MSH-biotin adduct was then captured with immobilized avidin and detected with anti-MSH antibody (biotin-capture ELISA) or was captured with immobilized anti-MSH antibody and detected with alkaline phosphatase-labelled avidin (MSH-capture ELISA). The MSH-capture ELISA was the most sensitive method, measuring as little as 0.3 fmol of MSH. Methods for biotinylating MSH directly from Mycobacterium spp. are described. The MSH-capture ELISA was tested for the detection of M. avium seeded in human urine or cerebrospinal fluid samples and for screening mutant M. smegmatis strains to detect MSH production.

L10 ANSWER 21 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 11

AN 2000:38115 BIOSIS

DN PREV200000038115

TI Glutathione and trypanothione in parasitic hydroperoxide metabolism.

AU Flohe, L. (1); Hecht, H. J.; Steinert, P.

CS (1) Department of Biochemistry, Technical University of Braunschweig, Mascheroder Weg 1, D-38124, Braunschweig Germany

SO Free Radical Biology & Medicine, (Nov., 1999) Vol. 27, No. 9-10, pp. 966-984.
ISSN: 0891-5849.

DT General Review

LA English

SL English

AB Thiol-dependent hydroperoxide metabolism in parasites is reviewed in respect to potential therapeutic strategies. The hydroperoxide metabolism of Crithidia fasciculata has been characterized to comprise a cascade of three enzymes, trypanothione reductase, tryparedoxin, and tryparedoxin peroxidase, plus two supportive enzymes to synthesize the redox mediator trypanothione from glutathione and spermidine. The essentiality of the system in respect to parasite vitality and virulence has been verified by genetic approaches. The system appears to be common to all genera of the Kinetoplastida. The terminal peroxidase of the system belongs to the protein family of peroxiredoxins which is also represented in Entamoeba and a variety of metazoan parasites. Plasmodial hydroperoxide metabolism displays similarities to the mammalian system in comprising glutathione biosynthesis, glutathione reductase, and at least one glutathione peroxidase homolog having the active site selenocysteine replacedby cysteine. Nothing precise is known about the antioxidant defence systems of Giardia, Toxoplasma, and Trichomonas species. Also, the role of ovothiols and ***mycothiols*** reportedly present in several parasites remains to be established. Scrutinizing known enzymes of parasitic antioxidant defence for suitability as drug targets leaves only those of the trypanosomatid system as directly or indirectly validated. By generally accepted criteria of target selection and feasibility considerations tryparedoxin and tryparedoxin peroxidase can at present be rated as the most appealing target structures for the development of antiparasitic drugs.

L10 ANSWER 22 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 12
AN 1999:449748 BIOSIS
DN PREV199900449748
TI Identification of the INO1 gene of Mycobacterium tuberculosis H37Rv reveals a novel class of inositol-1-phosphate synthase enzyme.
AU Bachhawat, Nandita (1); Mande, Shekhar C. (1)
CS (1) Institute of Microbial Technology, Sector 39A, Chandigarh, 160036 India
SO Journal of Molecular Biology, (Aug. 20, 1999) Vol. 291, No. 3, pp. 531-536.
ISSN: 0022-2836.
DT Article
LA English
SL English
AB 1L-myo-inositol (inositol) is vital for the biogenesis of ***mycothiol*** , phosphatidylinositol and glycosylphosphatidylinositol anchors linked to complex carbohydrates in Mycobacterium tuberculosis. All these cellular components are thought to play important roles in host-pathogen interactions and in the survival of the pathogen within the host. However, the inositol biosynthetic pathway in M. tuberculosis is not known. To delineate the pathways for inositol formation, we employed a unique combination of tertiary structure prediction and yeast-based functional assays. Here, we describe the identification of the gene for mycobacterial INO1 that encodes inositol-1-phosphate synthase distinct in many respects from the eukaryotic analogues.

L10 ANSWER 23 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 13
AN 1999:148924 BIOSIS
DN PREV199900148924
TI Characterization of Mycobacterium smegmatis mutants defective in 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside and ***mycothiol*** biosynthesis.
AU Newton, Gerald L.; Unson, Mia D.; Anderberg, Sara J.; Aguilera, Joseph A.; Oh, Nancy N.; Delcardayre, Stephen B.; Av-Gay, Yossef; Fahey, Robert C. (1)
CS (1) Dep. Chem. Biochemistry, Univ. California, San Diego, La Jolla, CA 92093 USA
SO Biochemical and Biophysical Research Communications, (Feb. 16, 1999) Vol. 255, No. 2, pp. 239-244.
ISSN: 0006-291X.
DT Article
LA English
AB ***Mycothiol*** (MSH) is the major low molecular weight thiol in mycobacteria. Two chemical mutants with low MSH and one with no MSH (strain 49) were produced in Mycobacterium smegmatis mc2155 to assess the role of MSH in mycobacteria. Strain 49 was shown to not produce 1-D-myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (GlcN-Ins), an intermediate in MSH biosynthesis. Relative to the parent strain, mutant 49 formed colonies more slowly on solid media and was more sensitive to H2O2, and rifampin, but less sensitive to isoniazid. Complementation of mutant 49 with DNA from M. tuberculosis H37Rv partially restored production of GlcN-Ins and MSH, and resistance to H2O2, but largely restored colony

growth rate and sensitivity to rifampin and isoniazid. The results indicate that MSH and GlcN-Ins are not essential for in vitro survival of mycobacteria but may play significant roles in determining the sensitivity of mycobacteria to environmental toxins.

L10 ANSWER 24 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 14
AN 2000:48516 BIOSIS
DN PREV200000048516
TI Thiols in formaldehyde dissimilation and detoxification.
AU Duine, Johannis A. (1)
CS (1) Department of Microbiology and Enzymology, Delft University of Technology, Julianalaan 67, NL-2628 BC, Delft Netherlands
SO Biofactors, (1999) Vol. 10, No. 2-3, pp. 201-206.
ISSN: 0951-6433.
DT General Review
LA English
SL English
AB Glutathione is not a universal coenzyme for formaldehyde oxidation. MySH (***mycothiol*** , 1-O-(2'-(N-acetyl-L-cysteinyl)amido-2'-deoxy-0varies-D-glucopyranosyl)-D-myo-inositol) is GSH's counterpart as coenzyme in formaldehyde dehydrogenase from certain Gram-positive bacteria. However, formaldehyde dissimilation and detoxification not only proceed via thiol-dependent but also via thiol-independent dehydrogenases. The distinct structures and enzymatic properties of MySH-dependent and GSH-dependent formaldehyde dehydrogenases could provide clues for development of selective drugs against pathogenic Mycobacteria. It is to be expected that other new types of thiol-dependent formaldehyde dehydrogenases will be dis-covered in the future. Indications exist that the product of thiol-dependent formaldehyde oxidation, the thiol formate ester, is not only hydrolytically converted into thiol and formate but can also be oxidatively converted in some cases by a molybdoprotein aldehyde dehydrogenase into the corresponding carbonate ester, decomposing spontaneously into CO2 and the thiol.

L10 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2002 ACS
AN 1998:163492 CAPLUS
DN 128:213410
TI Modulators of nitrosative and oxidative stress for the treatment of disease
IN Stamler, Jonathan S.; Griffith, Owen W.
PA Duke University, USA; Medical College of Wisconsin Research Foundation, Inc.
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9808566	A1	19980305	WO 1997-US13876	19970813
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6057367	A	20000502	US 1997-852490	19970507
AU 9740542	A1	19980319	AU 1997-40542	19970813

EP 963219 A1 19991215 EP 1997-938149 19970813
R: CH, DE, ES, FR, GB, IT, LI, NL, SE
US 6180824 B1 20010130 US 1999-361167 19990727
US 6359004 B1 20020319 US 2000-690989 20001018
PRAI US 1996-25819P P 19960830
US 1997-852490 A 19970507
WO 1997-US13876 W 19970813
US 1999-361167 A1 19990727
AB Mammals are treated for infections or for conditions assocd. with pathol. proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathol. proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2-8 carbon atoms, and the S-alkyl contains 1-10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g. humans at risk for a stroke because of having had a transient ischemic attack are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

L10 ANSWER 26 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 15
AN 1999:5037 BIOSIS
DN PREV199900005037
TI ***Mycothiol*** biosynthesis and metabolism: Cellular levels of potential intermediates in the biosynthesis and degradation of ***mycothiol*** in Mycobacterium smegmatis.
AU Anderberg, Sara J.; Newton, Gerald L.; Fahey, Robert C. (1)
CS (1) Dep. Chem. Biochem., Univ. Calif. at San Diego, La Jolla, CA 92093-0506 USA
SO Journal of Biological Chemistry, (Nov. 13, 1998) Vol. 273, No. 46, pp. 30391-30397.
ISSN: 0021-9258.
DT Article
LA English
AB ***Mycothiol*** (MSH; 1-D-myo-inosityl-2-(N-acetyl-L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (AcCys-GlcN-Ins)) is a novel thiol produced at millimolar levels by mycobacteria and other actinomycetes that do not make glutathione. We developed methods to determine the major components of MSH (AcCys, Cys-GlcN, AcCys-GlcN, Cys-GlcN-Ins, GlcN-Ins) in cell extracts. Mycobacterium smegmatis was shown to produce measurable levels (nmol/g of residual dry weight) of AcCys (apprx30), Cys-GlcN-Ins (apprx8), and GlcN-Ins (apprx100) but not Cys-GlcN (<3) or AcCys-GlcN (<80) during exponential growth in Middlebrook 7H9 medium. The level of GlcN-Ins declined 10-fold in stationary phase and apprx5-fold in 7H9 medium lacking glucose. Incubation in 10 mM AcCys produced 50- and 1000-fold increases in cellular Cys and AcCys levels, respectively, a 10-fold decrease in GlcN-Ins and a transient 3-fold increase in Cys-GlcN-Ins. These results exclude Cys-GlcN and AcCys-GlcN as intermediates in MSH biosynthesis and

implicate GlcN-Ins and Cys-GlcN-Ins as key intermediates. Assay of GlcN-Ins/ATP-dependent ligase activity with Cys and AcCys as substrates revealed that Cys was at least an order of magnitude better substrate. Based on the cellular measurements, MSH biosynthesis involves assembly of GlcN-Ins, ligation with Cys to produce Cys-GlcN-Ins, and acetylation of the latter to produce MSH.

L10 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 16
AN 1998:682990 CAPLUS
DN 130:81741
TI Synthesis of Des-myo-Inositol ***Mycothiol*** and Demonstration of a Mycobacterial Specific Reductase Activity
AU Patel, Mehul P.; Blanchard, John S.
CS Department of Biochemistry, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SO J. Am. Chem. Soc. (1998), 120(44), 11538-11539
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The kinetics and mechanistic characterization of the M. tuberculosis mycothione reductase is studied using substrate N-acetyl-L-cysteinyl-2-amino-2-deoxy-D-glucopyranoside disulfide, which was prepd. via coupling of .alpha.-D-glucosamine hydrochloride with N-.alpha.-Fmoc-S-acetamidomethyl-L-cysteine-pentafluorophenyl ester.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 28 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 17
AN 1998:386859 BIOSIS
DN PREV199800386859
TI An immunoassay for the detection and quantitative determination of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Davis, Charles; Fahey, Robert C. (1)
CS (1) Dep. Chem. and Biochem., Univ. Calif., San Diego, La Jolla, CA 92093 USA
SO Journal of Immunological Methods, (May 1, 1998) Vol. 214, No. 1-2, pp. 29-39.
ISSN: 0022-1759.
DT Article
LA English
AB ***Mycothiol*** (MSH) is a glycosylated derivative of V-acetylcysteine that may have antioxidant functions in mycobacteria and other actinomycetes. To develop a highly specific assay for MSH, we capitalized on the selective binding of thiols to a maleimide residue linked to bovine serum albumin and employed affinity-purified polyclonal antibody and an enzyme-linked secondary antibody for detection. The assay was shown to be specific and to detect MSH at levels as low as 0.1 pmol when conducted in the form of a microtiter plate-based ELISA. A similar, nitrocellulose membrane-based immunoassay was shown to be useful for qualitative detection of MSH-producing bacterial colonies.

L10 ANSWER 29 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 18

AN 1998:47007 BIOSIS
DN PREV199800047007
TI A Mycobacterium smegmatis mutant with a defective inositol monophosphate phosphatase gene homolog has altered cell envelope permeability.
AU Parish, Tanya; Liu, Jun; Nikaido, Hiroshi; Stoker, Neil G. (1)
CS (1) Dep. Infectious Tropical Diseases, London Sch. Hygiene and Tropical Med., Keppel St., London WC1E 7HT UK
SO Journal of Bacteriology, (Dec., 1997) Vol. 179, No. 24, pp. 7827-7833. ISSN: 0021-9193.
DT Article
LA English
AB A bacteriophage infection mutant (strain LIMP7) of Mycobacterium smegmatis was isolated following transposon mutagenesis. The mutant showed an unusual phenotype, in that all phages tested produced larger plaques on this strain compared to the parent strain. Other phenotypic characteristics of the mutant were slower growth, increased clumping in liquid culture, increased resistance to chloramphenicol and erythromycin, and increased sensitivity to isoniazid and several beta-lactam antibiotics. Permeability studies showed decreases in the accumulation of lipophilic molecules (norfloxacin and chenodeoxycholate) and a small increase with hydrophilic molecules (cephaloridine); taken together, these characteristics indicate an altered cell envelope. The DNA adjacent to the transposon in LIMP7 was cloned and was shown to be highly similar to genes encoding bacterial and mammalian inositol monophosphate phosphatases. Inositol is important in mycobacteria as a component of the major thiol ***mycothiol*** and also in the cell wall, with phosphatidylinositol anchoring lipoarabinomannan (LAM) in the cell envelope. In LIMP7, levels of phosphatidylinositol dimannoside, the precursor of LAM, were less than half of those in the wild-type strain, confirming that the mutation had affected the synthesis of inositol-containing molecules. The impA gene is located within the histidine biosynthesis operon in both M. smegmatis and Mycobactetium tuberculosis, lying between the hisA and hisF genes.

L10 ANSWER 30 OF 38 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 1998:408889 SCISEARCH
GA The Genuine Article (R) Number: ZK302
TI The biosynthesis of ***mycothiol***
AU Steenkamp D J (Reprint); Jardine A M; Bornemann C; Spies H S C
CS UNIV CAPE TOWN, SCH MED, ZA-7700 RONDEBOSCH, SOUTH AFRICA; UNIV STELLENBOSCH, NMR LAB, ZA-7600 STELLENBOSCH, SOUTH AFRICA
CYA SOUTH AFRICA
SO FASEB JOURNAL, (31 JUL 1997) Vol. 11, No. 9, Supp. [S], pp. 3420-3420. Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.
DT Conference; Journal
FS LIFE
LA English
REC Reference Count: 0

L10 ANSWER 31 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:422685 BIOSIS
DN PREV199799721888
TI The biosynthesis of ***mycothiol*** .
AU Steenkamp, Daniel J.; Jardine, Anwar M.; Borneman, Claus; Spies, Hendrik

S. C.
CS Chemical Pathol., Univ. Cape Town Medical Sch., Univ. Stellenbosch, Cape Town South Africa
SO FASEB Journal, (1997) Vol. 11, No. 9, pp. A1441.
Meeting Info.: 17th International Congress of Biochemistry and Molecular Biology in conjunction with the Annual Meeting of the American Society for Biochemistry and Molecular Biology San Francisco, California, USA August 24-29, 1997
ISSN: 0892-6638.
DT Conference; Abstract
LA English

L10 ANSWER 32 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 19
AN 1997:402392 BIOSIS
DN PREV199799708595
TI Biosynthesis of ***mycothiol*** : Elucidation of the sequence of steps in Mycobacterium smegmatis.
AU Bornemann, Claus; Jardine, M. Anwar; Spies, Hendrik S. C.; Steenkamp, Daniel J. (1)
CS (1) Dep. Chemical Pathol., Univ. Cape Town Med. Sch., Observatory 7925 South Africa
SO Biochemical Journal, (1997) Vol. 325, No. 3, pp. 623-629.
ISSN: 0264-6021.
DT Article
LA English
AB Several members of the Actinomycetales, including the medically important mycobacteria, produce 1-D-myo-inosityl-2-(N-acetyl-L-cysteinyl)amino-2-deoxy-alpha-D-glucopyranoside (trivial name ***mycothiol***) as their principal low-molecular-mass thiol. The pseudo-disaccharide component of ***mycothiol*** , 1-D-Myo-inosityl-2-amino-2-deoxy-alpha-D-glucopyranoside (alpha-D-GI), was synthesized by ligation of 1-D,L-2,3,4,5,6-penta-O-acetyl-myo-inositol to 3,4,6-tri-O-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-alpha-D-glucopyranosyl bromide to give, in the first instance, an isomeric mixture of alpha- and beta-linked pseudo-disaccharides. The alpha-coupled D,D and D,L isomers, alpha-D-GI and alpha-L-GI respectively, were purified from the mixture by TLC, followed by removal of the protecting groups. A cell-free extract of Mycobacterium smegmatis catalysed the ligation of cysteine, acetate and alpha-D-GI in the presence of ATP and Mg-2+ to form ***mycothiol*** , as judged by HPLC. When no acetate was added to the incubation mixture, an additional thiol accumulated. In the presence of (14C)acetate no radiolabel was recovered in this species, but only in ***mycothiol*** . The additional thiol was isolated as the bimane derivative, and 1H and 1H-1H COSY NMR spectra confirmed its identity as desacetylmycothiol. A more complete conversion of desacetylmycothiol into ***mycothiol*** was achieved in the presence of acetyl-S-CoA. These results indicate that the biosynthesis of ***mycothiol*** proceeds by the sequential addition of cysteine and acetate to alpha-D-GI. The inositol moiety appears to be an important determinant of specificity, since alpha-L-GI was poorly utilized.

L10 ANSWER 33 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 20
AN 1997:452192 BIOSIS

DN PREV199799751395
TI ***Mycothiol*** -dependent formaldehyde dehydrogenase, a prokaryotic medium-chain dehydrogenase/reductase, phylogenetically links different eukaryotic alcohol dehydrogenases: Primary structure, conformational modelling and functional correlations.
AU Norin, Annika; Van Ophem, Peter W.; Piersma, Sander R.; Persson, Bengt; Duine, Johannis A.; Jornvall, Hans (1)
CS (1) Dep. Med. Biochem. Biophysics, Karolinska Inst., S-171 77 Stockholm Sweden
SO European Journal of Biochemistry, (1997) Vol. 248, No. 2, pp. 282-289. ISSN: 0014-2956.
DT Article
LA English
AB Prokaryotic ***mycothiol*** -dependent formaldehyde dehydrogenase has been structurally characterized by peptide analysis of the 360-residue protein chain and by molecular modelling and functional correlation with the conformational properties of zinc-containing alcohol dehydrogenases. The structure is found to be a divergent medium-chain dehydrogenase/reductase (MDR), at a phylogenetic position intermediate between the cluster of dimeric alcohol dehydrogenases of all classes (including the human forms), and several tetrameric reductases/dehydrogenases. Molecular modelling and functionally important residues suggest a fold of the ***mycothiol*** -dependent formaldehyde dehydrogenase related overall to that of MDR alcohol dehydrogenases, with the presence of the catalytic and structural zinc atoms, but otherwise much altered active-site relationships compatible with the different substrate specificity, and an altered loop structure compatible with differences in the quaternary structure. Residues typical of glutathione binding class-III alcohol dehydrogenase are not present, consistent with that the ***mycothiol*** factor is not closely similar to glutathione. The molecular architecture is different from that of the 'constant' alcohol dehydrogenases (of class-III type) and the 'variable' alcohol dehydrogenases (of class-I and class-II types), further supporting the unique structure of ***mycothiol*** -dependent formaldehyde dehydrogenase. Borders of internal chain-length differences between this and other MDR enzymes coincide in different combinations, supporting the concept of limited changes in loop regions within this whole family of proteins.

L10 ANSWER 34 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 21
AN 1997:350023 BIOSIS
DN PREV199799649226
TI ***Mycothiol*** , 1-O-(2'-(N-acetyl-L-cysteinyl)amido-2'-deoxy-alpha-D-glucopyranosyl)-D-myo-inositol, is the factor of NAD/factor-dependent formaldehyde dehydrogenase.
AU Misset-Smits, Marijke; Van Ophem, Peter W.; Sakuda, Shohei; Duine, Johannis A. (1)
CS (1) Dep. Microbiol. Enzymol., Delft Univ. Technol., 2628 BC Delft Netherlands
SO FEBS Letters, (1997) Vol. 409, No. 2, pp. 221-222. ISSN: 0014-5793.
DT Article
LA English
AB Two different NAD/coenzyme-dependent formaldehyde dehydrogenases exist,

the well-known NAD/GSH-dependent (EC 1.2.1.1) and the more recently discovered NAD/Factor dependent enzyme. The GSH-dependent one has been found in eukaryotes and Gram-negative bacteria, the Factor-dependent one in two different Gram-positive bacteria. Previous work also showed that Factor and GSH are not interchangeable in the enzymatic reactions. Here it is revealed that the Factor is identical to ***mycothiol*** (MySH), 1-O-(2'-(N-acetyl-L-cysteinyl)amido-2'-deoxy-alpha-D-glucopyranosyl)-D-myo-inositol, a thiol compound which has recently been detected in Actinomycetes. Thus, MySH is GSH's companion as it is the coenzyme for the enzyme which henceforth can be indicated as NAD/MySHdependent formaldehyde dehydrogenase.

L10 ANSWER 35 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 22

AN 1996:232911 BIOSIS

DN PREV199698797040

TI Distribution of thiols in microorganisms: ***Mycothiol*** is a major thiol in most actinomycetes.

AU Newton, Gerald L.; Arnold, Karen; Price, Mitchel S.; Sherrill, Christopher; Delcardayre, Stephen B.; Aharonowitz, Yair; Cohen, Gerald; Davies, Julian; Fahey, Robert C. (1); Davis, Charles

CS (1) Dep. Chemistry, University California, San Diego, La Jolla, CA 92093-0506 USA

SO Journal of Bacteriology, (1996) Vol. 178, No. 7, pp. 1990-1995. ISSN: 0021-9193.

DT Article

LA English

AB ***Mycothiol*** (2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranosyl-(1 fwdarw 1)-myo-inositol) (MSH) has recently been identified as a major thiol in a number of actinomycetes (S. Sakuda, Z.-Y. Zhou, and Y. Yamada, Biosci. Biotech. Biochem. 58:1347-1348, 1994; H. S. C. Spies and D. J. Steenkamp, Eur. J. Biochem. 224:203213, 1994; and G. L. Newton, C. A. Bewley, T. J. Dwyer, R. Horn, Y. Aharonowitz, G. Cohen, J. Davies, D. J. Faulkner, and R. C. Fahey, Eur. J. Biochem. 230:821-825, 1995). Since this novel thiol is more resistant than glutathione to heavy-metal ion-catalyzed oxidation, it seems likely to be the antioxidant thiol used by aerobic gram-positive bacteria that do not produce glutathione (GSH). In the present study we sought to define the spectrum of organisms that produce MSH. GSH was absent in all actinomycetes and some of the other gram-positive bacteria studied. Surprisingly, the streptococci and enterococci contained GSH, and some strains appeared to synthesize it rather than import it from the growth medium. MSH was found at significant levels in most actinomycetes examined. Among the actinobacteria four Micrococcus species produced MSH, but MSH was not found in representatives of the Arthrobacter, Agromyces, or Actinomyces genera. Of the nocardioforms examined, Nocardia, Rhodococcus, and Mycobacteria spp. all produced MSH. In addition to the established production of MSH by streptomycetes, we found that Micromonospora, Actinomadura, and Nocardiopsis spp. also synthesized MSH.
Mycothiol production was not detected in Propionibacterium acnes or in representative species of the Listeria, Staphylococcus, Streptococcus, Enterococcus, Bacillus, and Clostridium genera. Examination of representatives of the cyanobacteria, purple bacteria, and spirochetes also gave negative results, as did tests of rat liver, bonito, Candida albicans, Neurospora crassa, and spinach leaves. The results, which

indicate that MSH production is restricted to the actinomycetes, could have significant implications for the detection and treatment of infections with actinomycetes, especially those caused by mycobacteria.

L10 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 23
AN 1995:630956 CAPLUS
DN 124:140470
TI The structure of U17 isolated from Streptomyces clavuligerus and its properties as an antioxidant thiol
AU Newton, Gerald L.; Bewley, Carole A.; Dwyer, Tammy J.; Horn, Ronda; Aharonowitz, Yair; Cohen, Gerald; Davies, Julian; Faulkner, D. John; Fahey, Robert C.
CS Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506, USA
SO Eur. J. Biochem. (1995), 230(2), 821-5
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB The predominant low-mol.-mass thiol produced by streptomycetes is a cysteine deriv. previously designated as U17. In this study the elucidation of the structure of the monobromobimane deriv. of U17 (I) is reported, which establishes the structure of U17 as 2-(N-acetylcysteinyl)amido-2-deoxy-.alpha.-D-glucopyranosyl-myo-inositol. The presence of the N-acetylcysteine moiety was indicated by formation of N-acetylcysteine-monobromobimane during acid hydrolysis of I. Complete hydrolysis of I released 1 mol glucosamine/mol cysteine as detd. by carbohydrate and amino acid anal. High-resoln. mass spectral anal. gave a precise mass consistent with the mol. formula C27H40N4O14S. Anal. of 13C-NMR, 1-dimensional 1H-NMR and 2-dimensional NMR expts. identified the remaining C6H12O6 moiety as myo-inositol, confirmed the presence of N-acetyl-cysteine and glucosamine, and established the connectivity of the components. Two chem. properties of this novel thiol, which is equated to ***mycothiol*** from Mycobacterium bovis, make it suitable as an intracellular storage form of cysteine and as an antioxidant thiol. First, it undergoes heavy-metal-ion catalyzed autoxidn. at a rate dramatically lower than that for cysteine and markedly lower than that for glutathione or N-acetylcysteine. Secondly, the .alpha.-(1.fwdarw.1) glycosidic link between glucosamine and myo-inositol is resistant to acid hydrolysis, hydrolyzing at a rate comparable to that of the 2 amide bonds in the mol.

L10 ANSWER 37 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:147933 BIOSIS
DN PREV199598162233
TI ***Mycothiol*** and ***mycothioldisulfide*** reductase from mycobacteria.
AU Steenkamp, Daniel J. (1); Spies, Hendrik S. C.; Rumbak, Elaine (1)
CS (1) Dep. Chem. Pathol., Univ. Cape Town Med. Sch., Cape Town South Africa
SO Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19B, pp. 70.
Meeting Info.: Keystone Symposium on Molecular Mechanisms in Tuberculosis Tamarron, Colorado, USA February 19-25, 1995
ISSN: 0733-1959.
DT Conference
LA English

L10 ANSWER 38 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 24
AN 1994:483653 BIOSIS
DN PREV199497496653
TI Thiols of intracellular pathogens: Identification of ovothiol A in Leishmania donovani and structural analysis of a novel thiol from Mycobacterium bovis.
AU Spies, Hendrik S. C.; Steenkamp, Daniel J. (1)
CS (1) Dep. Chemical Pathol., Univ. Cape Town Med. Sch., Observatory 7915 South Africa
SO European Journal of Biochemistry, (1994) Vol. 224, No. 1, pp. 203-213. ISSN: 0014-2956.
DT Article
LA English
AB Leishmania donovani, the causative agent of visceral leishmaniases, is an intracellular pathogen which proliferates within the host macrophages. Analysis of the thiol composition of L. donovani by means of the thiol-specific reagent, 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin, indicated that this organism produces substantial amounts of ovothiol A. This observation was further substantiated by HPLC of extracts of L. donovani after derivatization with bromobimane. L. donovani extracts contained a thiol, the bimane derivative of which had identical retention time and fluorescence quenching to a thiol from Crithidia fasciculata, which had previously been identified as ovothiol A. By comparison, the intracellular bacterial pathogen, Mycobacterium bovis, contained only one major low-molecular-mass thiol, which was assigned the trivial name ***mycothiol*** . The structure of the bimane derivative of ***mycothiol*** was solved by a combination of one- and two-dimensional 1H and 13C NMR spectroscopy. Spatial relationships in the molecule were further refined by NOE experiments and allowed identification of ***mycothiol*** as 1-D-myo-inositol-2-(N-acetyl-L-cysteinyl)amino-2-deoxy-alpha-D-glucopyranoside. This assignment was confirmed by positive-ion fast-atom-bombardment mass spectrometry which gave m/z = 677.6 Da and a sodiated species at 699.6 Da. Analysis of the dansylated hydrolysis products of performic-acid-oxidized ***mycothiol*** indicated the presence of 0.85 mol glucosamine and 1.02 mol cysteic acid/mol sulfhydryl groups. Crude extracts of M. bovis contained an enzyme which catalysed the NAD(P)H-2-dependent reduction of ***mycothiol*** disulfide to the free thiol. Analysis of perchloric acid extracts of Mycobacterium tuberculosis H37RV indicated the presence of a thiol which comigrated with ***mycothiol*** , both as the free thiol and as the 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin and bimane derivatives, on reverse-phase HPLC. The significance of these findings in terms of the evasion of the host defense mechanisms by leishmania parasites and mycobacteria is considered.

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L11 8 L10 AND ANTIBOD?

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YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1999:310093 BIOSIS
DN PREV199900310093
TI Improved methods for immunoassay of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Arnold, Karen F.; Davis, Charles E.; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506 USA
SO Journal of Clinical Microbiology, (July, 1999) Vol. 37, No. 7, pp. 2153-2157.
ISSN: 0095-1137.
DT Article
LA English
SL English
AB Improved enzyme-linked immunosorbent assay (ELISA) methods have been developed for the determination of femtomole amounts of ***mycothiol*** (MSH), the main low-molecular-weight thiol in mycobacteria. The immunoassays utilize an affinity-purified rabbit polyclonal ***antibody*** that is highly specific for the pseudodisaccharide moiety of MSH. MSH was first biotinylated by the thiol-specific reagent 3-(N-maleimidopropionyl)biocytin. The MSH-biotin adduct was then captured with immobilized avidin and detected with anti-MSH ***antibody*** (biotin-capture ELISA) or was captured with immobilized anti-MSH ***antibody*** and detected with alkaline phosphatase-labelled avidin (MSH-capture ELISA). The MSH-capture ELISA was the most sensitive method, measuring as little as 0.3 fmol of MSH. Methods for biotinylating MSH directly from Mycobacterium spp. are described. The MSH-capture ELISA was tested for the detection of M. avium seeded in human urine or cerebrospinal fluid samples and for screening mutant M. smegmatis strains to detect MSH production.
TI Improved methods for immunoassay of ***mycothiol*** .
AB Improved enzyme-linked immunosorbent assay (ELISA) methods have been developed for the determination of femtomole amounts of ***mycothiol*** (MSH), the main low-molecular-weight thiol in mycobacteria. The immunoassays utilize an affinity-purified rabbit polyclonal ***antibody*** that is highly specific for the pseudodisaccharide moiety of MSH. MSH was first biotinylated by the thiol-specific reagent 3-(N-maleimidopropionyl)biocytin. The MSH-biotin adduct was then captured with immobilized avidin and detected with anti-MSH ***antibody*** (biotin-capture ELISA) or was captured with immobilized anti-MSH ***antibody*** and detected with alkaline phosphatase-labelled avidin (MSH-capture ELISA). The MSH-capture ELISA was the most sensitive method, measuring as little as. . .
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Chemicals & Biochemicals
avidin; ***mycothiol***

L11 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:386859 BIOSIS
DN PREV199800386859
TI An immunoassay for the detection and quantitative determination of ***mycothiol*** .
AU Unson, Mia D.; Newton, Gerald L.; Davis, Charles; Fahey, Robert C. (1)
CS (1) Dep. Chem. and Biochem., Univ. Calif., San Diego, La Jolla, CA 92093 USA

SO Journal of Immunological Methods, (May 1, 1998) Vol. 214, No. 1-2, pp. 29-39.
ISSN: 0022-1759.
DT Article
LA English
AB ***Mycothiol*** (MSH) is a glycosylated derivative of V-acetylcysteine that may have antioxidant functions in mycobacteria and other actinomycetes. To develop a highly specific assay for MSH, we capitalized on the selective binding of thiols to a maleimide residue linked to bovine serum albumin and employed affinity-purified polyclonal ***antibody*** and an enzyme-linked secondary ***antibody*** for detection. The assay was shown to be specific and to detect MSH at levels as low as 0.1 pmol when conducted in the form of a microtiter plate-based ELISA. A similar, nitrocellulose membrane-based immunoassay was shown to be useful for qualitative detection of MSH-producing bacterial colonies.
TI An immunoassay for the detection and quantitative determination of ***mycothiol*** .
AB ***Mycothiol*** (MSH) is a glycosylated derivative of V-acetylcysteine that may have antioxidant functions in mycobacteria and other actinomycetes. To develop a. . . capitalized on the selective binding of thiols to a maleimide residue linked to bovine serum albumin and employed affinity-purified polyclonal ***antibody*** and an enzyme-linked secondary ***antibody*** for detection. The assay was shown to be specific and to detect MSH at levels as low as 0.1 pmol. . .
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Chemicals & Biochemicals
mycothiol -carrier protein conjugates: preparation;
mycothiol : antioxidant, purification, quantitative analysis;
polyclonal ***antibody*** : preparation

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:923972 CAPLUS
DN 136:66199
TI Mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with analytical and antimicrobial inhibitor design uses
IN Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, San Diego, USA; University of British Columbia
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001096529	A2	20011220	WO 2001-US19091	20010614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-211612P P 20000614

AB The present invention provides a family of bacterial acetylglucosaminylinositol deacetylases (MshB) with deacetylase activity against acylglucosaminylinositol and which play a key role in ***mycothiol*** biosynthesis. The invention deacetylases are characterized by a conserved 100 amino acid N-terminal region and 3 highly conserved histidine-contg. regions and by having deacetylase activity as well as amide hydrolase activity. The invention further provides methods for using the invention deacetylases in drug screening assays to det. compds. that inhibit activity. The invention provides for treatment of actinomycete infections in mammals using antibiotics that inhibit prodn. or activity of MshB and thereby reduce the prodn. of ***mycothiol*** and the virulence of the infecting bacteria.

TI Mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with analytical and antimicrobial inhibitor design uses

AB The present invention provides a family of bacterial acetylglucosaminylinositol deacetylases (MshB) with deacetylase activity against acylglucosaminylinositol and which play a key role in ***mycothiol*** biosynthesis. The invention deacetylases are characterized by a conserved 100 amino acid N-terminal region and 3 highly conserved histidine-contg. regions and by having deacetylase activity as well as amide hydrolase activity. The invention further provides methods for using the invention deacetylases in drug screening assays to det. compds. that inhibit activity. The invention provides for treatment of actinomycete infections in mammals using antibiotics that inhibit prodn. or activity of MshB and thereby reduce the prodn. of ***mycothiol*** and the virulence of the infecting bacteria.

ST acetylglucosaminylinositol deacetylase amidase gene mshB Mycobacterium; sequence acetylglucosaminylinositol deacetylase gene mshB Mycobacterium; antibiotic design screening acetylglucosaminylinositol deacetylase; ***mycothiol*** biosynthesis Acetinomycetes acetylglucosaminylinositol deacetylase

IT High throughput screening
(for inhibitor identification; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT Colorimetric indicators
Fluorescent indicators
(high-throughput screening for inhibitors; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mshB; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT Actinomyces israelii
Actinomycetes
Amycolatopsis mediterranei
Amycolatopsis orientalis
Antimicrobial agents

Corynebacterium diphtheriae
DNA sequences
Drug design
Drug screening
Molecular cloning
Mycobacterium abscessus
Mycobacterium africanum
Mycobacterium avium
Mycobacterium bovis
Mycobacterium chelonae
Mycobacterium intracellulare
Mycobacterium leprae
Mycobacterium marinum
Mycobacterium scrofulaceum
Mycobacterium smegmatis
Mycobacterium tuberculosis
Mycobacterium ulcerans
Protein sequences
Saccharopolyspora erythraea
Streptomyces coelicolor
Streptomyces lavendulae
Streptomyces lincolnensis
Streptomyces rochei
(mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT ***Antibodies***
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT Antisense oligonucleotides
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 340703-87-9, N-Acetyl-1-D-myo-inosityl-2-amino-2-deoxy-..alpha.-D-glucopyranoside deacetylase
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(342632-23-9; mycobacterial acetylglucosaminylinositol deacetylase ***is*** a mycothiol biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 382661-55-4
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 382661-50-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 382607-09-2 382661-51-0 382661-52-1 382661-53-2 382661-54-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(conserved domain fragment; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 38183-12-9, Fluorescamine 148757-94-2, 6-Aminoquinolyl-N-hydroxysuccinimidyl carbamate
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorometric marker for inhibitor screening; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 382657-48-9 382657-49-0 382657-50-3 382657-51-4 382657-52-5 382657-53-6 382657-54-7 382657-55-8 382657-56-9 382657-57-0 382657-58-1
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(inhibitor; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 7439-96-5, Manganese, biological studies 7440-02-0, Nickel, biological studies 7440-43-9, Cadmium, biological studies 7440-48-4, Cobalt, biological studies 7440-66-6, Zinc, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metal ion required for activity; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 340722-51-2
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(substrate activity; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 7512-17-6, N-Acetylglucosamine 192126-76-4, ***Mycothiol*** 382657-44-5 382657-45-6 382657-46-7 382657-47-8 383365-45-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrate activity; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 382661-77-0, 9: PN: WO0196529 SEQID: 8 unclaimed DNA 382661-78-1, 10: PN: WO0196529 SEQID: 9 unclaimed DNA 382661-79-2 382661-80-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

IT 382661-81-6 382661-82-7 382661-83-8
RL: PRP (Properties)
(unclaimed protein sequence; mycobacterial acetylglucosaminylinositol deacetylase is a ***mycothiol*** biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 2001:435230 CAPLUS
DN 135:57858
TI Bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification
IN Newton, Gerald L.; Av-gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042422	A2	20010614	WO 2000-US33232	20001207
WO 2001042422	A3	20020110		
AU 2001020702	A5	20010618	AU 2001-20702	20001207

PI WO 2001042422 A2 20010614 WO 2000-US33232 20001207
WO 2001042422 A3 20020110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001020702 A5 20010618 AU 2001-20702 20001207
PRAI US 1999-169503P A2 19991207
WO 2000-US33232 W 20001207
AB The present invention provides a family of bacterial acyl glucosaminyl inositol amidases with amidase activity against S-conjugate amides, particularly ***mycothiol*** -derived S-conjugate amides. The invention amidases are characterized by a highly conserved 20 amino acid N-terminal region and four highly conserved histidine-contg. regions and by having amidase activity, particularly amide hydrolase activity. Purifn., characterization and sequences of ***mycothiol*** S-conjugate amidases of Mycobacterium smegmatis mc2 155 and M. tuberculosis H37Rv (Rv1082) are disclosed. The invention further provides methods for using the invention amidases in drug screening assays to det. compds. with antibiotic activity or compds. that inhibit activity or prodn. of endogenous acyl glucosaminylinositol amidase in bacteria. The invention further provides methods for detoxifying a toxic substance by contacting the toxic substance with an invention amidase, for example, by expression of the amidase under environmental conditions in a bacterium.
TI Bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification
AB The present invention provides a family of bacterial acyl glucosaminyl inositol amidases with amidase activity against S-conjugate amides, particularly ***mycothiol*** -derived S-conjugate amides. The invention amidases are characterized by a highly conserved 20 amino acid N-terminal region and four highly conserved histidine-contg. regions and by having amidase activity, particularly amide hydrolase activity. Purifn., characterization and sequences of ***mycothiol*** S-conjugate amidases of Mycobacterium smegmatis mc2 155 and M. tuberculosis H37Rv (Rv1082) are disclosed. The invention further provides methods for using

the invention amidases in drug screening assays to det. compds. with antibiotic activity or compds. that inhibit activity or prodn. of endogenous acyl glucosaminylinositol amidase in bacteria. The invention further provides methods for detoxifying a toxic substance by contacting the toxic substance with an invention amidase, for example, by expression of the amidase under environmental conditions in a bacterium.

ST bacteria acyl glucosaminyl inositol amidase drug screening detoxification; Mycobacterium ***mycothiol*** conjugate amidase sequence drug screening detoxification

IT Bacteria (Eubacteria)
(antibiotic-producing; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT mRNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense oligonucleotides against; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Actinomycetes
Amycolatopsis mediterranei
Amycolatopsis orientalis
Antibacterial agents
Corynebacterium diphtheriae
DNA sequences
Drug screening
Environmental pollution
Gene therapy
Molecular cloning
Mycobacterium africanum
Mycobacterium bovis
Mycobacterium chelonae
Mycobacterium intracellulare
Mycobacterium leprae
Mycobacterium marinum
Mycobacterium smegmatis
Mycobacterium tuberculosis
Protein sequences
Saccharopolyspora erythraea
Streptomyces coelicolor
Streptomyces lavendulae
Streptomyces lincolnensis
Streptomyces rochei
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT ***Antibodies***
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Antisense oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug

screening and detoxification)

IT Detoxification
(biol.; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Antibiotic resistance
(decreasing of; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Antibiotics
(fermn. of; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(fragments; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Hydrocarbons, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(halo; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT Fermentation
(of antibiotics; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 344970-61-2P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 208784-93-4P, Amidase, ***mycothiol*** S-conjugate (Mycobacterium tuberculosis gene Rv1082) 342632-23-9P, Amidase, ***mycothiol*** S-conjugate 344325-15-1P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 75802-23-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); USES (Uses)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 192126-76-4D, ***Mycothiol*** , S-conjugates 340722-51-2

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 75-01-4, Vinyl chloride, biological studies 78-79-5, Isoprene, biological studies 79-01-6, Trichloroethene, biological studies 106-93-4, 1,2-Dibromoethane 107-06-2, 1,2-Dichloroethane, biological studies 127-18-4, Perchloroethene, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 616-91-1, Mercapturic acid
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 344920-15-6 345225-14-1 345225-17-4 345225-23-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 343433-36-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 344970-62-3
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 344970-60-1 344972-91-4, 12: PN: WO0142422 SEQID: 9 unclaimed DNA 344972-92-5 344972-93-6
RL: PRP (Properties)
(unclaimed nucleotide sequence; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 344972-90-3
RL: PRP (Properties)
(unclaimed protein sequence; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

IT 170561-41-8 206283-11-6 208788-02-7 344972-94-7 344972-95-8
RL: PRP (Properties)
(unclaimed sequence; bacterial ***mycothiol*** S-conjugate amidase and other enzymes of acyl glucosaminyl inositol amidase family and their use for drug screening and detoxification)

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1999:297325 CAPLUS
DN 130:322691
TI Reagents and immunoassay for the detection and quantitative determination of ***mycothiol*** and precursors thereof
IN Fahey, Robert C.; Newton, Gerald L.; Unson, Maria Margarita D.; Davis, Charles E.; Angerberg, Sara J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9921580	A1	19990506	WO 1998-US22577	19981023
AU 9911988	A1	19990517	AU 1999-11988	19981023

PI WO 9921580 A1 19990506 WO 1998-US22577 19981023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9911988 A1 19990517 AU 1999-11988 19981023
PRAI US 1997-63620P P 19971027
WO 1998-US22577 W 19981023
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting ***mycothiol*** or precursor thereof. An ***antibody*** is provided which binds to ***mycothiol*** or a ***mycothiol*** precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of ***mycothiol*** or a precursor thereof. A method is provided for detecting ***mycothiol*** or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of ***mycothiol*** or precursor thereof in a sample.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Reagents and immunoassay for the detection and quantitative determination of ***mycothiol*** and precursors thereof
AB A method of detecting a member of the taxa actinomycetes is provided. A method also is provided for detecting ***mycothiol*** or precursor thereof. An ***antibody*** is provided which binds to ***mycothiol*** or a ***mycothiol*** precursor. A method is further provided for diagnosis of a subject having or at risk of having an actinomycetes-assocd. disorder. A method is also provided for identifying a sample with altered prodn. of ***mycothiol*** or a precursor thereof. A method is provided for detecting ***mycothiol*** or precursor thereof in a bacterial colony. Kits are also disclosed which are useful for detecting the presence of ***mycothiol*** or precursor thereof in a sample.
ST reagent immunoassay ***mycothiol*** precursor

IT Actinomycetes
Animal tissue
Ascites
Bacteria (Eubacteria)
Blood analysis
Body fluid
Cerebrospinal fluid
Diagnosis
Feces
Immunoassay
Mycobacterium
Pleural fluid
Sputum
Test kits
Urine analysis
(reagents and immunoassay for detection and quant. detn. of ***mycothiol*** and precursors)
IT ***Antibodies***
Monoclonal ***antibodies***
Reagents
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reagents and immunoassay for detection and quant. detn. of ***mycothiol*** and precursors)
IT Respiratory tract
(secretion; reagents and immunoassay for detection and quant. detn. of ***mycothiol*** and precursors)
IT 75802-23-2 192126-76-4, ***Mycothiol*** 192126-76-4D, ***Mycothiol*** , precursors 195389-17-4 223902-58-7
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(reagents and immunoassay for detection and quant. detn. of ***mycothiol*** and precursors)
IT 71418-44-5, Monobromobimane 148757-94-2, 6-Aminoquinolyl-N-hydroxysuccinimidyl carbamate
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reagents and immunoassay for detection and quant. detn. of ***mycothiol*** and precursors)

L11 ANSWER 6 OF 8 USPATFULL
AN 2002:57833 USPATFULL
TI Manipulating nitrosative stress to upregulate nitrosative stress defenses
IN Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States
PA Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin, Milwaukee, WI, United States (U.S. corporation)
PI US 6359004 B1 20020319
AI US 2000-690989 20001018 (9)
RLI Continuation of Ser. No. US 1999-361167, filed on 27 Jul 1999, now patented, Pat. No. US 6180824 Division of Ser. No. US 1997-852490, filed on 7 May 1997, now patented, Pat. No. US 6057367
PRAI US 1996-25819P 19960830 (60)
DT Utility
FS GRANTED

EXNAM Primary Examiner: Weddington, Kevin E.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3105
AB Mammals are treated for infections or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and the S-alkyl- contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.
SUMM . . . other biochemical pathways to protect themselves from nitrosative stress. Thiols (e.g., glutathione in mammals and glutathione-producing helminths and microorganisms, L-homocysteine, ***mycothiol*** , ovothiols, etc.) and enzymes which mediate constitutive thiol synthesis comprise the first line of defense. Antinitrosative stress genes and their. . .
DETD . . . glutathione-producing bacteria, such as E. coli and Salmonella); trypanothione in trypanosomas, L-homocysteine in Salmonella typhimurium and other bacteria containing L-homocysteine; ***mycothiol*** in ***mycothiol*** -producing microorganisms (including ***mycothiol*** -producing bacteria, such as actinomycetes (which cause, for example, mycobacteria tuberculosis), Nocardia asteroides, Nocardia brasiliensis and other Nocardia species (which cause,. . .
DETD . . . or in pathologic helminths or in pathologically proliferating mammalian cells, inhibitors of trypanothione synthesis, inhibitors of L-homocysteine synthesis, inhibitors of ***mycothiol*** synthesis, inhibitors of the synthesis of ovothiols, and inhibitors of synthesis of .delta.-(L-.alpha.-aminoadipoyl)-L-cysteinyl-D-valine.
DETD Selective depleters of thiol useful herein, include, for example, selective glutathione depleters, trypanothione depleters, L-homocysteine depleters, ***mycothiol*** depleters, and .delta.-(L-.alpha.-aminoadipoyl)-L-cysteinyl-D-valine depleters.
DETD Selective inhibitors of glutathione synthesis for use in treating helminth caused infections include, for example, antihelminth ***antibody*** cross-linked by ester linkage to thiol synthesis inhibitor such as L-buthionine-S-sulfoximine. The antiproliferative effective amount, i.e., the dosage normally ranges. . .
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.mu.g to. . .

DETD Selective inhibitors of glutathione synthesis for use in inhibiting proliferation of pathologically proliferating cancer cells, include, for example, an antitumor ***antibody*** (i.e., to an epitope on a cancer cell) cross-linked by ester. linkage to thiol synthesis inhibitor such as L-buthionine-S-sulfoximine. The. . .

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DETD ***Mycothiol*** (described in Newton, G. L., et al., J. Bacteriol, 178, 1990-1995 (1996)) protects against nitrosative stress in ***mycothiol*** -producing microbes, e.g., Mycobacter and Actinomycetes. ***Mycothiol*** does not protect against nitrosative stress in mammals. Thus, inhibitors of ***mycothiol*** synthesis and depleters of ***mycothiol*** are administered herein to selectively inhibit growth (proliferation) of ***mycothiol*** -producing microbes in mammals with infections caused thereby.

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DETD . . . antisense construct to a heat shock protein or mRNA. The inhibitors are made selective, for example, by attachment to antihelminth ***antibody*** and are administered intravenously at a dosage of 1 .mu.g to 100 mg.

DETD . . . growth of the helminth. The inhibitor is aminotriazole which is made selective by cross-linking by an amide linkage to antihelminth ***antibody*** and is administered intravenously at a dosage of 10 .mu.g to 100 mg/kg mammalian body weight per day.

DETD . . . of pathologically proliferating cancer cells, the agents are made selective by local delivery or by attachment to a tumor specific ***antibody*** or by other strategies for local delivery well-known in the drug delivery art and are administered intravenously at a dosage. .
.

DETD . . . For inhibiting proliferation of pathologically proliferating cancer cells, aminotriazole is made selective by cross-linking by an amide linkage to antitumor ***antibody*** (i.e., to an epitope of a cancer cell) and the selective agent is administered intravenously at a dosage of 10. . .

DETD . . . are made selective by local delivery or, in the case of proliferating cancer cells, by attachment to a tumor specific ***antibody*** . In the former case, they may be administered from a stent or an implant pellet where they are present in. . .

DETD . . . calcium ionophors. Selectivity is obtained in application to

inhibiting the proliferation of pathologically proliferating cancer cells by attachment to antitumor ***antibody*** (i.e., to an epitope of a cancer cell) and dosage of the ***antibody*** plus agent is 10 .mu.g to 100 mg/kg mammalian body weight per day and the route of administration is intravenous.. . .

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DETD . . . in pathologically proliferating cancer cells are the same manipulators of nitrosative stress described to have this function hereinbefore, e.g., antitumor ***antibody*** cross-linked by ester linkage to L-buthionine-s-sulfoximine, and the dosages and routes of administration are the same as those discussed hereinbefore.. . . administration described above in conjunction with these agents may be used for these agents in this embodiment, or are antitumor ***antibodies*** to which have been attached nitrosative stress agents as described above utilized with the dosages and routes of administration described. . .

DETD . . . hepatosplenomegaly. Diagnosis is made by eggs of S. japonicum found in the stool. The patient is given anti S. japonicum ***antibody*** cross-linked by ester linkage to L-buthionine-S-sulfoximine I.V. at a dose of 500 mg for one day together with praziquantel (60. . .

L11 ANSWER 7 OF 8 USPATFULL

AN 2001:14679 USPATFULL

TI Manipulating nitrosative stress to kill pathologic microbes, pathologic helminths and pathologically, proliferating cells or to upregulate nitrosative stress defenses

IN Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States

PA Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin, Milwaukee, WI, United States (U.S. corporation)

PI US 6180824 B1 20010130

AI US 1999-361167 19990727 (9)

RLI Division of Ser. No. US 1997-852490, filed on 7 May 1997, now patented, Pat. No. US 6057367

PRAI US 1996-25819P 19960830 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Weddington, Kevin E.

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Mammals are treated for infection or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and the S-alkyl- contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

SUMM . . . other biochemical pathways to protect themselves from nitrosative stress. Thiols (e.g., glutathione in mammals and glutathione-producing helminths and microorganisms, L-homocysteine, ***mycothiol*** , ovothiols, etc.) and enzymes which mediate constitutive thiol synthesis comprise the first line of defense. Antinitrosative stress genes and their. . .

DETD . . . glutathione-producing bacteria, such as E. coli and Salmonella); trypanothione in trypanosomas, L-homocysteine in Salmonella typhimurium and other bacteria containing L-homocysteine; ***mycothiol*** in ***mycothiol*** -producing microorganisms (including ***mycothiol*** -producing bacteria, such as actinomycetes (which cause, for example, mycobacteria tuberculosis), Nocardia asteroides, Nocardia brasiliensis and other Nocardia species (which cause,. . .

DETD . . . or in pathologic helminths or in pathologically proliferating mammalian cells, inhibitors of trypanothione synthesis, inhibitors of L-homocysteine synthesis, inhibitors of ***mycothiol*** synthesis, inhibitors of the synthesis of ovothiols, and inhibitors of synthesis of .delta.-(L-.alpha.-aminoadipoyl)-L-cysteinyl-D-valine.

DETD Selective depleters of thiol useful herein, include, for example, selective glutathione depleters, trypanothione depleters, L-homocysteine depleters, ***mycothiol*** depleters, and .delta.-(L-.alpha.-aminoadipoyl)-L-cysteinyl-D-valine depleters.

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DETD . . . of pathologically proliferating cancer cells, the agents are made selective by local delivery or by attachment to a tumor specific ***antibody*** or by other strategies for local delivery well-known in the drug delivery art and are administered intravenously at a dosage. . .

DETD . . . For inhibiting proliferation of pathologically proliferating cancer cells, aminotriazole is made selective by cross-linking by an amide linkage to antitumor ***antibody*** (i.e., to an epitope of a cancer cell) and the selective agent is administered intravenously at a dosage of 10. . .

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L11 ANSWER 8 OF 8 USPATFULL
AN 2000:54150 USPATFULL
TI Manipulating nitrosative stress to kill pathologic microbes, pathologic helminths and pathologically proliferating cells or to upregulate nitrosative stress defenses
IN Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States
PA Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin Research Foundation, Inc., Milwaukee, WI, United States (U.S. corporation)
PI US 6057367 20000502
AI US 1997-852490 19970507 (8)
PRAI US 1996-25819P 19960830 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Weddington, Kevin E.
CLMN Number of Claims: 66
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3415
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Mammals are treated for infections or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and the S-alkyl-contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

SUMM . . . other biochemical pathways to protect themselves from nitrosative stress. Thiols (e.g., glutathione in mammals and glutathione-producing helminths and microorganisms, L-homocysteine, ***mycothiol*** , ovothiols, etc.) and enzymes which mediate constitutive thiol synthesis comprise the first line of defense. Antinitrosative stress genes and their. . .

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DETD . . . For inhibiting proliferation of pathologically proliferating cancer cells, aminotriazole is made selective by cross-linking by an amide linkage to antitumor ***antibody*** (i.e., to an epitope of a cancer cell) and the selective agent is administered intravenously at a dosage of 10. . .

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DETD . . . calcium ionophors. Selectivity is obtained in application to inhibiting the proliferation of pathologically proliferating cancer cells by attachment to antitumor ***antibody*** (i.e., to an epitope of a cancer cell) and dosage of the ***antibody*** plus agent is 10 .mu.g to 100 mg/kg mammalian body weight per day and the route of

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DETD . . . in pathologically proliferating cancer cells are the same manipulators of nitrosative stress described to have this function hereinbefore, e.g., antitumor ***antibody*** cross-linked by ester linkage to L-buthionine-S-sulfoximine, and the dosages and routes of administration are the same as those discussed hereinbefore.. . . administration described above in conjunction with these agents may be used for these agents in this embodiment, or are antitumor ***antibodies*** to which have been attached nitrosative stress agents as described above utilized with the dosages and routes of administration described. . .

DETD . . . hepatosplenomegaly. Diagnosis is made by eggs of S. japonicum found in the stool. The patient is given anti S. japonicum ***antibody*** cross-linked by ester linkage to L-buthionine-S-sulfoximine I.V. at a dose of 500 mg for one day together with praziquantel (60. . .

CLM What is claimed is:

. . . wherein the inhibition is carried out on the pathologic microbes and the manipulator of nitrosative stress is an inhibitor of ***mycothiol*** synthesis or a depleter of ***mycothiol*** in the pathologic microbes.

10. The method of claim 9 wherein the inhibitor of ***mycothiol*** synthesis or depleter of ***mycothiol*** is a transportable nitrosylated peptide.

=> s 1-d-myo-inosityl-2-amino-2-deoxy-?-d-glucopyranoside
ADDITIONAL CHARACTERS REQUIRED AFTER '?' FOR LEFT TRUNCATION
ADDITIONAL CHARACTERS REQUIRED AFTER '?' FOR LEFT TRUNCATION
ADDITIONAL CHARACTERS REQUIRED AFTER '?' FOR LEFT TRUNCATION
ADDITIONAL CHARACTERS REQUIRED AFTER '?' FOR LEFT TRUNCATION
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ADDITIONAL CHARACTERS REQUIRED AFTER '?' FOR LEFT TRUNCATION
Additional characters must follow the left truncation symbol in your search term. If your search term contains a punctuation mark before the truncation symbol and you are searching in a field that uses

implied proximity, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index. To see which fields in the current file have left truncation, enter "HELP SFIELDS" at an arrow prompt (=>).

=> s 1-d-myo-inosityl-2-amino-2-deoxy-X-d-glucopyranoside
L12 0 1-D-MYO-INOSITYL-2-AMINO-2-DEOXY-X-D-GLUCOPYRANOSIDE

<------User Break------>
u
SEARCH ENDED BY USER
SEARCH ENDED BY USER

=> s 1-d-myo-inosityl-2-amino-2-deoxy?
L13 24 1-D-MYO-INOSITYL-2-AMINO-2-DEOXY?

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 5 DUP REM L13 (19 DUPLICATES REMOVED)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:923972 CAPLUS
DN 136:66199
TI Mycobacterial acetylglucosaminylinositol deacetylase is a mycothiol biosynthetic enzyme with analytical and antimicrobial inhibitor design uses
IN Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C.
PA The Regents of the University of California, San Diego, USA; University of British Columbia
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001096529	A2	20011220	WO 2001-US19091	20010614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-211612P P 20000614
AB The present invention provides a family of bacterial acetylglucosaminylinositol deacetylases (MshB) with deacetylase activity against acylglucosaminylinositol and which play a key role in mycothiol biosynthesis. The invention deacetylases are characterized by a conserved

100 amino acid N-terminal region and 3 highly conserved histidine-contg. regions and by having deacetylase activity as well as amide hydrolase activity. The invention further provides methods for using the invention deacetylases in drug screening assays to det. compds. that inhibit activity. The invention provides for treatment of actinomycete infections in mammals using antibiotics that inhibit prodn. or activity of MshB and thereby reduce the prodn. of mycothiol and the virulence of the infecting bacteria.

IT 340703-87-9, N-Acetyl- ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -..alpha.-D-glucopyranoside deacetylase
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(342632-23-9; mycobacterial acetylglucosaminylinositol deacetylase is a mycothiol biosynthetic enzyme with anal. and antimicrobial inhibitor design uses)

L14 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2000:439612 BIOSIS
DN PREV200000439612
TI A novel mycothiol-dependent detoxification pathway in mycobacteria involving mycothiol S-conjugate amidase.
AU Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C. (1)
CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093 USA
SO Biochemistry, (September 5, 2000) Vol. 39, No. 35, pp. 10739-10746. print. ISSN: 0006-2960.
DT Article
LA English
SL English
AB Mycothiol, 1-D-myo-inosityl-2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (MSH), is composed of N-acetylcysteine (AcCys) amide linked to ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside (GlcN-Ins) and is the major thiol produced by most actinomycetes. When Mycobacterium smegmatis was treated with the alkylating agent monobromobimane (mBBr), the cellular mycothiol was converted to its bimane derivative (MSmB). The latter was rapidly cleaved to produce GlcN-Ins and the bimane derivative of N-acetylcysteine (AcCySmB), a mercapturic acid that was rapidly exported from the cells into the medium. The other product of cleavage, GlcN-Ins, was retained in the cell and utilized in the resynthesis of mycothiol. The mycothiol S-conjugate amidase (amidase) responsible for cleaving MSmB was purified to homogeneity from M. smegmatis. A value of Km = 95 +- 8 muM and a value of kcat = 8 s-1 was determined for the amidase with MSmB as substrate. Activity with 100 muM mycothiol or with the monobromobimane derivative of 1-D-myo-inosityl-2-(L-cysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (CySmB-GlcN-Ins) or of 2-(N-acetyl-L-cysteinyl)amido-2-deoxy-(alpha,beta)-D-glucopyranoside (AcCySmB-GlcN) was at least 103 lower than with 100 muM MSmB, demonstrating that the amidase is highly specific for S-conjugates of mycothiol. Conjugates of mycothiol with the antibiotic cerulenin, N-ethylmaleimide, 3-(N-maleimidopropionyl)-biocytin, and 7-diethylamino-3-(4'-maleimidylphenyl)-4-methylcoumarin also exhibited significant activity. The sequence of the amino-terminal 20 residues was

determined, and an open reading frame (Rv1082) coding for 288 residues having an identical predicted amino-terminal amino acid sequence was identified in the Mycobacterium tuberculosis genome. The Rv1082 gene (mca) from M. tuberculosis was cloned and expressed in Escherichia coli, and the expressed protein was shown to have substrate specificity similar to the amidase from M. smegmatis. These results indicate that mycothiol and mycothiol S-conjugate amidase play an important role in the detoxification of alkylating agents and antibiotics.

AB Mycothiol, 1-D-myo-inosityl-2-(N-acetylcysteinyl)amido-2-deoxy-alpha-D-glucopyranoside (MSH), is composed of N-acetylcysteine (AcCys) amide linked to ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside (GlcN-Ins) and is the major thiol produced by most actinomycetes. When Mycobacterium smegmatis was treated with the alkylating agent monobromobimane. . .

L14 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

AN 2001:313790 BIOSIS

DN PREV200100313790

TI N-acetyl- ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside deacetylase (MshB) is a key enzyme in mycothiol biosynthesis.

AU Newton, Gerald L.; Av-Gay, Yossef; Fahey, Robert C. (1)

CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0506: rcfahey@ucsd.edu USA

SO Journal of Bacteriology, (December, 2000) Vol. 182, No. 24, pp. 6958-6963. print.
ISSN: 0021-9193.

DT Article

LA English

SL English

AB Mycothiol is a novel thiol produced only by actinomycetes and is the major low-molecular-weight thiol in mycobacteria. Mycothiol was previously shown to be synthesized from ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside by ligation with cysteine followed by acetylation. A novel mycothiol-dependent detoxification enzyme, mycothiol conjugate amidase, was recently identified in Mycobacterium smegmatis and shown to have a homolog, Rv1082, in Mycobacterium tuberculosis. In the present study we found that a protein encoded by the M. tuberculosis open reading frame Rv1170, a homolog of Rv1082, possesses weak mycothiol conjugate amidase activity but shows substantial deacetylation activity with 1-D-myo-inosityl-2-acetamido-2-deoxy-alpha-D-glucopyranoside (GlcNAc-Ins), a hypothetical mycothiol biosynthetic precursor. The availability of this protein enabled us to develop an assay for GlcNAc-Ins, which was used to demonstrate that GlcNAc-Ins is present in M. smegmatis at a level about twice that of mycothiol. It was shown that GlcNAc-Ins is absent in mycothiol-deficient mutant strain 49 of M. smegmatis and that this strain can concentrate GlcNAc-Ins from the medium and convert it to mycothiol. This demonstrates that GlcNAc-Ins is a key intermediate in the pathway of mycothiol biosynthesis. Assignment of Rv1170 as the gene coding the deacetylase in the M. tuberculosis genome represents the first identification of a gene of the mycothiol biosynthesis pathway. The presence of a large cellular pool of substrate

for this enzyme suggests that it may be important in regulating mycothiol biosynthesis.

TI N-acetyl- ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside deacetylase (MshB) is a key enzyme in mycothiol biosynthesis.

AB. . . produced only by actinomycetes and is the major low-molecular-weight thiol in mycobacteria. Mycothiol was previously shown to be synthesized from ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside by ligation with cysteine followed by acetylation. A novel mycothiol-dependent detoxification enzyme, mycothiol conjugate amidase, was recently identified in Mycobacterium. . .

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Molecular Genetics (Biochemistry and Molecular Biophysics); Metabolism

IT Chemicals & Biochemicals
1-D-myo-inosityl-2-acetamido-2-deoxy-alpha-D-glucopyranoside; N-acetyl- ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside deacetylase [MshB]; mycothiol; mycothiol conjugate amidase

RN 340703-87-9 (N-ACETYL- ***1*** - ***D*** - ***MYO*** - ***INOSITYL*** - ***2*** - ***AMINO*** - ***2*** - ***DEOXY*** -ALPHA-D-GLUCOPYRANOSIDE DEACETYLASE)
192126-76-4 (MYCOTHIOL)

L14 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3

AN 1999:148924 BIOSIS

DN PREV199900148924

TI Characterization of Mycobacterium smegmatis mutants defective in ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside and mycothiol biosynthesis.

AU Newton, Gerald L.; Unson, Mia D.; Anderberg, Sara J.; Aguilera, Joseph A.; Oh, Nancy N.; Delcardayre, Stephen B.; Av-Gay, Yossef; Fahey, Robert C. (1)

CS (1) Dep. Chem. Biochemistry, Univ. California, San Diego, La Jolla, CA 92093 USA

SO Biochemical and Biophysical Research Communications, (Feb. 16, 1999) Vol. 255, No. 2, pp. 239-244.
ISSN: 0006-291X.

DT Article

LA English

AB Mycothiol (MSH) is the major low molecular weight thiol in mycobacteria. Two chemical mutants with low MSH and one with no MSH (strain 49) were produced in Mycobacterium smegmatis mc2155 to assess the role of MSH in mycobacteria. Strain 49 was shown to not produce ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside (GlcN-Ins), an intermediate in MSH biosynthesis. Relative to the parent strain, mutant 49 formed colonies more slowly on solid media and was more sensitive to H2O2, and rifampin, but less sensitive to isoniazid. Complementation of mutant 49 with DNA from M. tuberculosis H37Rv partially restored production of GlcN-Ins and MSH, and resistance to H2O2, but largely restored colony growth rate and sensitivity to rifampin and isoniazid. The results indicate that MSH and

GlcN-Ins are not essential for in vitro survival of mycobacteria but may play significant roles in determining the sensitivity of mycobacteria to environmental toxins.

TI Characterization of Mycobacterium smegmatis mutants defective in ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside and mycothiol biosynthesis.

AB. . . produced in Mycobacterium smegmatis mc2155 to assess the role of MSH in mycobacteria. Strain 49 was shown to not produce ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside (GlcN-Ins), an intermediate in MSH biosynthesis. Relative to the parent strain, mutant 49 formed colonies more slowly on solid media. . .

IT Major Concepts
Metabolism

IT Chemicals & Biochemicals
hydrogen peroxide; mycothiol: biosynthesis; rifampin; ***1*** - ***D*** - ***myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -&a-D-glucopyranoside: biosynthesis

L14 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4

AN 1997:402392 BIOSIS

DN PREV199799708595

TI Biosynthesis of mycothiol: Elucidation of the sequence of steps in Mycobacterium smegmatis.

AU Bornemann, Claus; Jardine, M. Anwar; Spies, Hendrik S. C.; Steenkamp, Daniel J. (1)

CS (1) Dep. Chemical Pathol., Univ. Cape Town Med. Sch., Observatory 7925 South Africa

SO Biochemical Journal, (1997) Vol. 325, No. 3, pp. 623-629. ISSN: 0264-6021.

DT Article

LA English

AB Several members of the Actinomycetales, including the medically important mycobacteria, produce 1-D-myo-inosityl-2-(N-acetyl-L-cysteinyl)amino-2-deoxy-alpha-D-glucopyranoside (trivial name mycothiol) as their principal low-molecular-mass thiol. The pseudo-disaccharide component of mycothiol, ***1*** - ***D*** - ***Myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside (alpha-D-GI), was synthesized by ligation of 1-D,L-2,3,4,5,6-penta-O-acetyl-myo-inositol to 3,4,6-tri-O-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-alpha-D-glucopyranosyl bromide to give, in the first instance, an isomeric mixture of alpha- and beta-linked pseudo-disaccharides. The alpha-coupled D,D and D,L isomers, alpha-D-GI and alpha-L-GI respectively, were purified from the mixture by TLC, followed by removal of the protecting groups. A cell-free extract of Mycobacterium smegmatis catalysed the ligation of cysteine, acetate and alpha-D-GI in the presence of ATP and Mg-2+ to form mycothiol, as judged by HPLC. When no acetate was added to the incubation mixture, an additional thiol accumulated. In the presence of (14C)acetate no radiolabel was recovered in this species, but only in mycothiol. The additional thiol was isolated as the bimane derivative, and 1H and 1H-1H COSY NMR spectra confirmed its identity as desacetylmycothiol. A more complete conversion of desacetylmycothiol into mycothiol was achieved in the presence of acetyl-S-CoA. These results indicate that the biosynthesis

of mycothiol proceeds by the sequential addition of cysteine and acetate to alpha-D-GI. The inositol moiety appears to be an important determinant of specificity, since alpha-L-GI was poorly utilized.

AB. . . including the medically important mycobacteria, produce 1-D-myo-inosityl-2-(N-acetyl-L-cysteinyl)amino-2-deoxy-alpha-D-glucopyranoside (trivial name mycothiol) as their principal low-molecular-mass thiol. The pseudo-disaccharide component of mycothiol, ***1*** - ***D*** - ***Myo*** - ***inosityl*** - ***2*** - ***amino*** - ***2*** - ***deoxy*** -alpha-D-glucopyranoside (alpha-D-GI), was synthesized by ligation of 1-D,L-2,3,4,5,6-penta-O-acetyl-myo-inositol to 3,4,6-tri-O-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-alpha-D-glucopyranosyl bromide to give, in the first instance, an isomeric mixture of. . .

IT Miscellaneous Descriptors
BIOCHEMISTRY AND BIOPHYSICS; BIOSYNTHESIS; METABOLISM; MOLECULAR STRUCTURE; MYCOTHIOL; ***1*** - ***D*** - ***MYO*** - ***INOSITYL*** - ***2*** - ***AMINO*** - ***2*** - ***DEOXY*** -ALPHA-D-GLUCOPYRANOSIDE

=> s 1-d-myo-inosityl-2-(l0cystinyl)amido-2-deoxy?
MISSING OPERATOR 'NOSITYL-2-(L0CYSTINYL'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s 1-d-myo-inosityl-2-l0 cystinyl amido-2-deoxy?
L15 0 1-D-MYO-INOSITYL-2-L0 CYSTINYL AMIDO-2-DEOXY?